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PROBLEMS OF SPACE BIOLOGY, VOL. 50 NYSTAGMOMETRY FOR EVALUATION OF THE STATUS OF THE VESTIBULAR FUNCTION

M. M. Levashov

Translation of "Problemy kosmicheskoy biologii, Tom 50. Nistagmometriya v otsenke sostoyaniya vestibulyarnoy funktsii, Edited by V. A. Kislyakov, Leningrad, Nauka Press, Leningrad Branch, 1984, pp 1-221

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16. Abstract

The book is devoted to various aspects of nystagmometry, primarily those in which the study of nystagmus serves as a means to learn about the vestibular apparatus. Along with exhaustive published material, the monograph presents data from many years of research by the author on the physiological mechanisms of nystagmus, the features of nystagmus when vestibular stimulation is combined with optokinetic, the role of vestibular afferentation asymmetry in the asymmetry of reactions to optokinetic stimulus, a nystagmometric approach to studying the hydrodynamic interaction among semicircular canals, as well as several other questions. A great deal of attention is given to methods of recording nystagmus, calibrating nystagmograms, quantitative evaluation of nystagmographic material, new nystagmometric characteristics and diagnostic techniques. A diagnostic model is proposed which makes it possible to obtain important information on the condition of the vestibular system from results of vestibular testing.

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FOREWORD

The function of the nonaural labyrinth-vestibular apparatus discovered by P. F. Fleurance in the beginning of the 19th century first attracted researchers' attention in terms of pure science. In time it was determined that the vestibular apparatus consists of two sections. In addition to the system of semicircular canals already known from the work of P. Fleurance, a system of otolithic organs which respond to the effects of linear acceleration and to changes in position in the field of gravitation was discovered. It was revealed that these two systems interact (I. Breyer, R. Magnus, V. I. Voyachek, K. L. Chilov). The broadening and deepening knowledge of the physiology and morphology of the vestibular system attracted clinicians to the pathology of this organ, which led to development of corresponding specialties: otorhinolaryngology and otoneurology (R. Barany, P. Menier). V. I. Voyachek studied the importance of the human vestibular function in terms of the development of aviation. He proposed a set of vestibular procedures which were incorporated into aviation medicine practice and then developed further (I. I. Bryanov, Ye. M. Yuganov, et al.)

A new stage in the evolution of research on the vestibular system -- both experimental-theoretical and applied -- was reached with the conquest of outer space and manned space flights. The significance of this stage is evidenced by numerous national and international symposia devoted to the role of the vestibular system in ensuring spatial orientation and in an organism's statokinetic stability, and to discovering mechanisms of vestibular dysfunctions and their treatment in cosmonauts (O. G. Gazenko, A. Graybiel). Direct research on the vestibular function in animals in special biological satellites under conditions of weightlessness was expanded (Ya. A. Vinnikov, T. Gualtierotti). During this research, the search for ways to improve the accuracy of experimental procedures and the use of quantitative methods for evaluating reaction parameters were outlined. In particular, information on the impulse activity of primary utricular nerve afferents in an animal (a frog) on board a spacecraft was transmitted to Earth from a biological satellite and analyzed by computer in the "OFO-A" space experiment (T. Gualtierotti).

Of the numerous vestibular reactions, nystagmus deserves attention because of the clear correlation among its properties on the one hand and the unique features of the vestibular stimulus (planarity, magnitude, and sign of angular acceleration) on the other. This makes it possible to assess cupuloendolymphatic shifts in each functional pair of canals and the condition of the vestibular system overall. Representatives of various specialties are now involved in the study of nystagmus begun by the authorities in labyrinthology, P. Barany and V. I.

Voyachek. They are approaching the problem from different standpoints, refining a procedure for experimental research on the reaction, recording it and quantitatively evaluating it. A broad range of questions related to the study of nystagmus, which the author of this book proposes to identify by the term "nystagmometry," is closely connected to the problem of evaluating the condition of the vestibular system. It is precisely to this field of labyrinthology that M. M. Levashov has devoted his efforts.

This book combines a large amount of original and published data on the mechanisms of nystagmus and quantitative evaluations of this reaction's parameters, based on modern methods of nystagmography, mathematical statistics, and computer technology. One might expect that M. M. Levashov's monograph will be useful to a wide range of specialists involved in research and applied study in physiology, otorhinolaryngology, otoneurology, aviation and space medicine, etc. The research generalized in this monograph was begun and expanded at the I. P. Pavlov Institute for Physiology of the Academy of Sciences of the USSR and continued and concluded at the Leningrad Research Institute for Ear, Throat, Nose and Speech of the Ministry of Health of the RSFSR.

Dr. V. A. Kislyakov

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ABBREVIATIONS AND NOTATIONS

AFC (A_{FC})	- Fast component amplitude
ASC (A_{SC})	- Slow component amplitude
AF	- Afferent flow
AF_s	- Afferent flow (spontaneous)
BT	- Bithermal test
C	- Arithmetic mean of an individual nystagmometric characteristic
C_{int}	- Integrated arithmetic means for an individual nystagmometric characteristic
CC	- Cumulative curve
CN	- Caloric nystagmus
CS	- Calibration signal
CV	- Variational factor
DC	- Dynamic characteristic
DFC (T_{FC})	- Fast component duration
DPN	- Directional preponderance of the nystagmus
DR (T_R)	- Reaction duration
DSC (T_{SC})	- Slow component duration
d_1, d_2	- Quadratic form of deviations from the norm during comparison with data from an individual observed in terms of type 1 diagnosis or type 2 diagnosis
EC	- Elementary characteristic
EL	- Energy level (activity of the nuclear structure of a model)
ENG	- Electronystagmogram
EOG	- Electro-oculogram
F	- Nystagmic impulse frequency
FS	- Fast component
IA	- Inherent activity of the nuclear structure (in a model)
K_{DP}	- Directional preponderance factor in a bithermal test
K_{LA}	- Labyrinth asymmetry factor in a bithermal test
K_{TE}	- Thermostimulus efficiency factor in a bithermal test
K_r, K_l	- Factor for the proportionality between - nystagmus intensity and stimulus magnitude, or the slope of the AF characteristic (in a model); "r" and "l" indicate the sides
LA	- Labyrinth asymmetry
LP	- Latent period
$M_0(X)$, $M_1(X)$ $M_2(X)$	- Dynamic characteristic moments
m	- Mean sample error
N_{rw}, N_{rc} N_{lw}, N_{lc}	- Caloric nystagmus intensities (in a model; the stimulated side is labeled "r" (right) or "l" (left), the stimulus' sign "w" (warm) or "c" (cool)

NC_r, NC_l	- Vestibular nuclear structure (in a model); "r" - right, "l" - left.
NI (N)	- Number of impulses
OKN	- Optokinetic nystagmus
OKN_C	- Cortical optokinetic nystagmus
OKN_l	- Leftward optokinetic nystagmus
OKN_r	- Rightward optokinetic nystagmus
OKN_S	- Subcortical optokinetic nystagmus
OKS	- Optokinetic stimulus
P	- Probability of error if affiliation with one set is refuted
p	- Probability of divergence from zero
RPN	- Reverse postoptokinetic nystagmus
RF	- Reticular formation
SC	- Slow component
SFC	- Fast component speed
SSC	- Slow component speed
$\bar{x}$	- Arithmetic mean for a sample
Δ	- Phonal difference in energy level of two nuclear structures (in a model)
σ	- Root-mean-square (standard) deviation for a sample.
TC	- Total characteristic
TD	- Total duration of the nystagmus (LP + DR)
VN	- Vestibular nystagmus
VOKN	- Vestibulo-optokinetic nystagmus
VOKNC	- Vestibulooptokinetic coincident nystagmus
VPN	- Vestibular post-rotatory nystagmus
VRN	- Vestibular rotatory nystagmus

PROBLEMS OF SPACE BIOLOGY, VOL. 50
NYSTAGMOMETRY FOR EVALUATION OF THE STATUS
OF THE VESTIBULAR FUNCTION

M. M. Levashov

Introduction

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The vestibular apparatus is a multidimensional biological transformer of the mechanical energy of angular and linear acceleration into signals about body position and motion. Its multidimensional nature results from three pairs of semicircular canals, pairs of utriculi, and pairs of sacculi located in various planes of three-dimensional space. The vestibular apparatus is connected to nerve centers and efferent organs to form a multilevel system for controlling head and body position in space. The vestibular system performs this function in interaction with other sensory and efferent systems ([73], p. 29). This definition, given by physiologists and included in the textbook on normal physiology for universities [94], is complete enough. It is given here to show which trends in applied research of the vestibular system may be most promising and what role nystagmometry can play in this research.

The term "nystagmometry", as we suggest, means not only a direct procedure for measuring nystagmus (i.e. a procedure or even a group of procedures), but the entire broad range of problems related in some way to the study of nystagmus.

The need to classify these problems as a more or less independent branch of science has become obvious insofar as factual data has been compiled on mechanisms by which nystagmus develops and forms and, subsequently, on its diagnostic value. As early as 1927 the great Soviet otorhinolaryngologist V. I. Voyachek, in an extensive program report on the status of laryngology at the Second All-Union Conference of Otorhinolaryngologists [35], found it necessary to define a special field, "Nystagmology," and emphasized that research devoted to nystagmus is, as it were, a separate branch of science. The term "nystagmology" did not catch on in past decades because the study of nystagmus had not become a truly independent science. At the same time, the scope of knowledge about nystagmic reactions -- various forms of nystagmus, mechanisms, structures which bring about nystagmus, about the diagnostic value of reactions, about new means to study nystagmic reactions, et al. -- is a very important problem. At present we can assert with complete confidence that /8 there exists a certain set of theoretical and applied research and analysis, related by a common object of study -- nystagmus,

*Numbers in the margin indicate pagination of the foreign text.

as well as a quantitative approach to studying nystagmus, regardless of the specific goals and tasks (physiological, clinico-diagnostic, aerospace, cybernetic, etc.) and regardless of specific methodological conventions. It is exactly this set which it is suitable to identify by the special term "nystagmometry."

Given this definition, we can include a rather wide range of research and analyses (experimental, theoretical, applied, and technological) into nystagmometry, including those which are in some way related to studying the vestibular function. However, it would be mistaken to regard nystagmometry as a branch of vestibulology, since the study of nystagmus is not necessarily related to vestibular problems. Therefore nystagmometry has only partial application in vestibulology, which is just one field and can be characterized by the fact that, in it, the study of nystagmus is a means to study the vestibular system, i.e. nystagmus serves as a source of indirect information on this system.

Nystagmometry has long played an important role in vestibulology (both basic and applied). This is primarily because of the unique features which typify nystagmus. The most important feature of the nystagmic reaction is vectorality: the direction and plane of nystagmus are rather closely related to the properties of the stimulus acting on the vestibular apparatus. The relationships among the qualities of nystagmus and specific ampullar receptors in the semicircular canals which most actively participate in some way in its formation have been thoroughly studied. There exists information on the quantitative relationship between the characteristics of nystagmus and stimulus parameters. It is also important that a procedure exists which makes it possible to stimulate only one of the two labyrinths -- the caloric test. Finally, a simple and reliable procedure for recording nystagmus, suitable for everyday use, has become firmly established and has proven itself in practice -- electronystagmography.

If we return to the definition given at the very beginning, we can easily understand just how multidimensional vestibular dysfunctions can be when, by virtue of any sort of experimental effect or pathological process, any of the qualities inherent in the vestibular system change. It follows that, to obtain a more complete idea of the nature of vestibular dysfunction (i.e. the possible cause and mechanisms by which disturbances occur, the level on which they occurs, the dynamics of the damage, etc.), we need a comprehensive approach to studying the condition of the vestibular system [179]. The ideal approach would include an objective quantitative evaluation of each of the system's properties. Indeed, the partial loss of the ability to convert the mechanical energy of angular acceleration into signals on position in space, which turns the vestibular system into a source of disinformation, can be a

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dysfunction. Therefore, we need methods to discover such disturbances. One specific example of a manifestation of this type of disturbance is asymmetry in the function of paired receptor formations (at least until compensation begins). Further, this multidimensional nature, one of the basic properties of the vestibular system, also requires objective quantitative evaluation, since a dysfunction is possible even in this sense. Consequently, we need objective methods to study the function of not only the horizontal, but also the vertical semicircular canals, not to mention the otolithic organs. Finally, multilevel control, resulting from interaction with other systems, i.e. another very important feature of the vestibular system, also merits researchers' attention. We need tests suitable for discovery and objective quantitative evaluation of vestibular dysfunction from these standpoints also.

Nystagmometry must play a significant role in solving these diverse problems. Vestibulologists may be especially interested primarily in experimental research on mechanisms by which nystagmi form, on the basis of defining and comparing particular symptoms or properties of the reaction in the norm and in pathology, as well as in research devoted to development of diagnostic techniques and rules based on producing a nystagmic reaction and on quantitative evaluation of the latter.

Most often this research is directed by physiologists and pathophysiologists. They are dedicated to studying the roles of various structures in bringing about a reaction and to defining principles by which it develops given the unique features of the stimulus, given pharmacological effects, et al. Study of nystagmus to discover objective indications of the interaction of afferent systems, so necessary to analyzing three-dimensional orientation and statokinetic stability of a human in, for example, the severe conditions of space flight, is important in research in these fields. In particular, changes in nystagmus can be used to judge the mechanisms by which vision and vestibular systems affect each other, the interaction of various labyrinth sections (semicircular canals and otolithic apparatus), the effect of so-called extra-labyrinthine factors, etc. In most cases, such studies are done in experiments on animals, more rarely on healthy humans. Therefore they can be classified as experimental-theoretical nystagmometry.

One might say that there also exists applied nystagmometry, /10
i.e. the field of research specially devoted to developing and using quantitative approaches required for differential diagnosis, professional qualification, treatment efficiency evaluation, etc.

As regards work in applied research on the vestibular function, the ultimate goal of nystagmometry is, in most cases, diagnosis, i.e. obtaining an answer to the following set of

critical questions: Normal or pathological? If pathological, uni- or bilateral? Peripheral or central? Local or widespread? If local, how is the pathological process localized? What is the level of vestibular dysfunction (or compensation)? Obviously, all of these questions cannot be answered without in-depth nystagmometric research [18, 19], regardless of how complete the remaining vestibulometric testing is. Much remain unstudied in applied nystagmometry, and further research is required. We particularly need theoretical substantiation for several empirical techniques, optimized vestibulometric tests, etc.

Dividing nystagmometry into theoretical and applied categories is arbitrary at best. It is quite apparent that applied nystagmometry is based to a large extent on data from experimental-theoretical nystagmometry, while the latter in turn uses the wealth of clinical material as a source of unique information just as important and interesting for theory as that obtained in specially planned experiments on animals.

Unfortunately we are too often aware of the gap between basic and applied nystagmometric research. Eliminating this gap is an important task, since the development of functional and differential diagnoses, prognostications, etc. depends on progress in experimental-theoretical research. Theoretical research especially should help us to understand the principal capabilities of a procedure selected for some specific study. It is intended to present a picture of what information can and must be extracted from a nystagmogram, given a particular experiment or clinical study. This includes work to develop ideas of the mechanisms by which a stimulus acts on the vestibular system and the principles by which the stimulus needed to check a specific diagnostic hypothesis is selected if the latter is to be tested using a nystagmometric approach.

The wide range of problems which must be solved to ensure progress in nystagmometry can also include technological problems. Solving them in most cases is related to the level of technological development (electronics, automation, optics, computers) and the level to which technology has been implemented in biology and medicine. These tasks include development of precisely monitored methods for stimulating the vestibular apparatus, methods for reliably recording various types of nystagmus, automatic quantitative processing of nystagmometric data, and several more. Apparently, there are no essential technological problems in improving and automating nystagmometric research. The most common obstacles are that the very level of purely theoretical nystagmometric research is inadequate to formulate a particular assignment. In other words, experimental-technical nystagmometry should provide a proven approach to solving problems in applied (diagnostic) nystagmometry and should provide this approach through instrumentation. /11

Vestibular function is especially important in space biology and aerospace medicine, because acceleration and weightlessness, which impose increased and generally extraordinary requirements on the vestibular system, are among the factors to which an organism is exposed under flight conditions. Successfully overcoming the negative impact of these factors greatly depends on the level of knowledge about the physiology and pathology of the vestibular apparatus. Nystagmometry can contribute greatly to acquiring this knowledge, especially in the fields in which the study of nystagmus is the means to learn about mechanisms of the vestibular function.

Therefore, of the wide range of problems related to nystagmometry, this monograph includes those which can provide new information on the functioning of the vestibular apparatus itself and on the interaction of the vestibular system and other sensory systems and those which are related to improving the efficacy of vestibular diagnosis. Here diagnosis is used in the broadest sense. It is quite possible that so-called motion sickness, which some people never experience, but which strikes other in a particularly severe form, is to a certain extent associated in the latter group with an undefined vestibular dysfunction which never manifests itself in everyday life and does not hinder work under ordinary circumstances. Hence, diagnostic techniques which facilitate observation of extreme variants of the physiological norm or insignificant deviations during subclinical dysfunctions and are suitable for professional qualification and professional examinations are needed. It is now apparent that not enough research has been done to solve problems of this type using trapezoidal rotation testing or monothermal caloric testing. At the minimum, we need a bithermal test which permits recording of nystagmic reactions and quantitative evaluation of these reactions. A similar comment can be made in terms of optokinetic testing: a traditional test which uses an optokinetic drum and fixes the /12
subject's attention on a moving stimulus is suitable only to discovering obvious disturbances. Observing latent dysfunctions requires other procedures. In studying nystagmic reactions, it does matter which characteristics of the reaction are taken as external manifestations of vestibular system activity and how they are evaluated. For example, in studying labyrinth reactivity in terms of caloric tests, it is hardly worthwhile to evaluate nystagmus by measuring a characteristic such as reaction duration. The value of nystagmus frequency is also problematic in such work. This book is devoted to this and several other problems related to applying nystagmometry to the study of the vestibular function. It reviews both information borrowed from published literature and data obtained by the author in his own research and attempts to define certain promising trends in future nystagmometric research.

Chapter 1. Vestibulo-Oculomotor Reactions

Stimulation of the vestibular apparatus is associated with the reaction of all extra-ocular muscles, i.e. four direct (m. rectus lateralis, m. rectus medialis, m. rectus superior, m. rectus inferior) and two oblique (m. obliquus superior, m. obliquus inferior) in each eye. In addition, vestibular[531] (in the m. retractor bulbi), vestibulopalpebral[443], and vestibulopupillar [527, 529] reflexes are reported.

Of all the numerous vestibular reflexes, tonic and rhythmic vestibulomotor reactions are of greatest interest in applied vestibular tests. The first are related to the effect of linear accelerations and change in head orientation in the gravitational field on the vestibiluar apparatus; the second occur during angular accelerations.

Tonic Vestibulo-Oculomotor Reactions

Tonic concomitant eye deviations occur as a result of stimulation of otolithic apparatus receptors. In general, eye movement is intended to keep the position of the image of surrounding objects on the retina unchanged. For example, if the head moves forward, the eye shifts upward to the sagittal plane if frontal eye arrangement is characteristic of the given biological form. When the head of an animal with eyes arranged laterally tilts in this way, the eyes move around the optic axes -- the upper poles of the eyes shift caudally (cf. figure 1). Vertical tonic eye shifts in such animals occur if the head turns around the naso-occipital (sagittal) axis. If it tilts to the right, for example, the right eye is diverted upward, the left -- downward. Tonic vestibulo-oculomotor reactions have been described in detail by Magnuson [436], but study of this phenomenon is far from complete. For example, the relative involvement of the sacculus and utriculus in these reactions has not been finally determined. It has been shown in particular that no spontaneous eye deviation occurs in rabbits whose saccular membrane has been removed [572]. Nor does cutting one saccular nerve in a rabbit cause eye deviations if the head is in normal position, i.e. parietal up[487]. If the head turns around the naso-occipital axis, the effect depends on the direction of the tilt. If the affected ear has been turned upward, an ordinary deviation occurs, i.e. eye deviation in the frontal plane opposite to the tilt. If the tilt is toward the treated ear, there is no deviation /15
whatsoever. If the saccular nerves are severed bilaterally, there is also no eye deviation (for any head position). On the basis of these experiments it was concluded that eye deviations are a reflex from the sacculus and that the stimulating factor

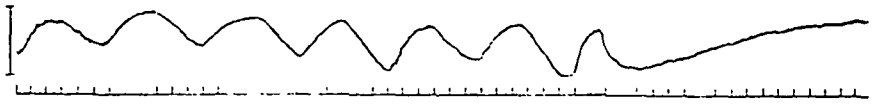

Figure 1. Tonic rotations of a rabbit's eye around the optic axis caused by periodic tilting of the head around the bitemporal axis to a horizontal position 30° lower.

Fragment of a record made using polarized light (cf. figure 24 and [125]). The descent of the line corresponds to turning the left eye clockwise. Calibration signal -- a deviation of ±10° from initial position; time interval -- 1 sec.

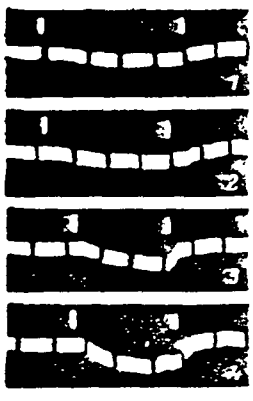

Figure 2. Tonic vestibulo-oculomotor reflex of a rabbit. Turning the right eye downward around the naso-occipital axis during rhythmic electrical stimulation of left vestibular receptors by a series of rectangular pulses lasting 0.2 msec (as per [111]).

Recordings were made by photonystagmographic method (cf. figure 17 and [108, 140]). Time intervals (breaks in the recording) - 500 msec. Arrows indicate the beginning and end of stimulation. Pulse tracking frequency: (1) 30, (2) 50, (3) 70, (4) 90 Hz.

is tension in the pili of the saccular macula, while pressure from the saccular membrane on macular pili causes no reaction, i.e. the vestibulo-oculomotor reflex from the sacculus is unidirectional. However, this study noted that, if the otolithic membrane of the sacculus was stimulated electrically, reaction direction depended on the electrical stimulus' sign. When the sacculus was stimulated by an anode, one eye deviated downward toward the stimulus, the other -- upward. With cathodic /16

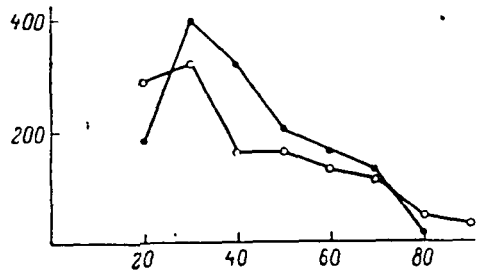

Figure 3. Latent period of tonic vestibulo-oculomotor reflex of a rabbit during rhythmic electrical stimulation of the vestibule receptor.

X-axis - impulse frequency, Hz; Y-axis - latent period in two experiments, msec (arithmetic means were calculated from several recordings at each stimulation frequency).

stimulation, there was also deviation, but in the opposite direction. It is easy to see the similarity of this phenomenon to the effect of polarizing the ampullar apparatus, when anode and cathode cause vestibulo-oculomotor reactions opposite in sign and similar to reflexes during utriculopetal or utriculofugal cupula deviations. There is direct evidence of the existence of bi-directional reflexes from the sacculus. Szentágothai [552] showed that, in a cat, mechanical deformation of the sacculus membrane, like natural deformations from lateral tilting of the head, are accompanied by vestibulo-oculomotor reactions, which are qualitatively similar to compensatory reactions. Results opposite in sign were obtained depending on the direction in which the membrane deformed.[1]

Utriculus receptors also take part in compensatory vertical deviation in a rabbit's eyes [111]. One eye shifts upward toward the stimulation, while that on the other side is diverted downward (cf. figure 2). Reflex parameters depend on electrical impulse frequency (cf. figure 3-5).

We should probably accept that there is a complex interaction between sacculus and utriculus receptors, in part involving duplication of function [432].

Semicircular canals also take part in reactions related to tilting the head. In real life conditions, their receptors are stimulated at the same time as otolithic organs. On the basis of stimulus parameters and features of the eye's motor reaction, we can talk only about primary stimulation of some part of the vestibular apparatus. After tilting ends, the tilted position is maintained by stimulating the otolithic apparatus.

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1 This information pertains only to vestibulo-oculomotor reactions. For the function of otolithic receptors, the importance of slipping, strain, and pressure mechanisms, see [77].

Superficially similar (e.g. in direction) extraocular muscle reflexes can result from the action of three factors in each labyrinth: cupula deviation, membranous labyrinth deformation, and otolithic membrane displacement[552]. The effects are distinguished by time characteristics -- latent period and duration. Thus, eye movement due to tilting the

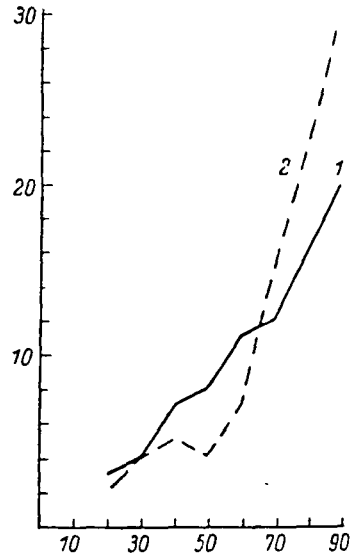

Figure 4. Amplitude of the tonic vestibulo-oculomotor reflex of a rabbit during rhythmic electrical stimulation of vestibule receptors. /17

X-axis -- impulse frequency, Hz; Y-axis -- amplitude (degrees) at which the eyeball turns around the naso-occipital axis in the same experiment at electrode voltage of (1) 30 and (2) 40 V.

head (i.e. during and after tilting) should be considered as a complex reaction consisting of three components with a direct transition from one to another.

When the head turns, the eye always moves in the plane of the stimulated semicircular canal (or canals) -- more precisely, in the plane in which the head turns. If vertical canals are stimulated, the eye is diverted depending on the optic axis position typical for that animal [550].

Detailed study of specific nerve connections which produce complex eye movements has become possible with the development of electrophysiological experiment technology. These studies provide a picture, for example, of the arrangement of specific paths along which exciting and inhibiting influences travel from first-order neurons in the rear semicircular canal to the ipsi- and counterlateral motoneurons in the extra-ocular muscles of a cat [566].

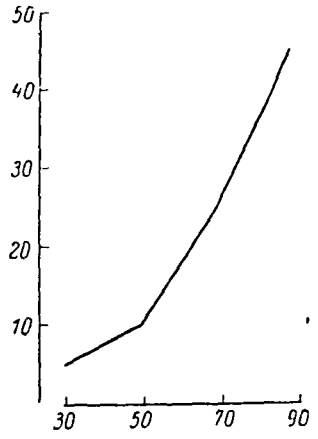

Figure 5. Angular velocity of the right eye of a rabbit downward around the naso-occipital axis during rhythmic stimulation of left vestibule receptors.

X-axis -- stimulation frequency, Hz; Y-axis -- angular velocity of eye movement, $^{\circ}\cdot sec^{-1}$.

The large number of combinations of vertical, horizontal, and rotatory (wheel-like) components of eye movement present well-known problems in applied research. Therefore, where detailed analysis of eye movements is not a subject of study, we are limited to quantifying the preponderant component of movement and ignoring the rest. There is rather great interest in rotatory movements [3, 93, 215, 388]. Study of otolithic reactions can apparently play a significant role in diagnosing labyrinth hydropsy [3]. It is important to measure tonic reflexes in vestibular tests in which otolithic organs interact with semicircular canals. Physiological experiments on rabbits in particular have demonstrated this [133, 187]. /18

Eye reflexes still play a very minor role in the system of applied vestibulometric research. One reason is that electro-oculographic procedure, i.e. the simplest and most common way to record rotatory eye movements, cannot be used, since rotation is around the electrical axis of the eye-dipole.

Rhythmic Vestibulo-Oculomotor Reaction -- Nystagmus

Nystagmus which occurs during rotation was first described by Purkin'ye, but the idea that it is vestibular in origin was preceded by observations by Fleurance, who noted rhythmic eye oscillations during experimental damage to semicircular canals (from [210]). Many years later, after Khedesh's [360, 361] and Ewald's [304] work, nystagmus was finally recognized as a specific vestibular reaction. As a result of numerous studies in which Soviet scientists [17, 32-35, 36, 56, 195, 211] played a significant role, the idea of vestibular nystagmus as a rhythmic variation of compensatory eye movements was formulated [195].

The term "vestibular nystagmus" (VN) is used here to designate a rhythmic vestibulo-oculomotor reaction occurring in response to stimulation (adequate or inadequate) of the ampullar apparatus. In otoneurological practice, where nystagmus is

often the spontaneous symptom of a pathological process, other terminology, "labyrinthine nystagmus," "vestibular trunk nystagmus," et al. is sometimes used [197].

In ontogenesis, vestibular nystagmus is last among vestibular reactions. For example, in rabbits, post-rotary nystagma occurs on the 9-10th day of life, while post-rotary arrhythmic eye diversion takes place as early as the 4th-6th days [155, 156]. Quantitative characteristics of nystagmus are subject to change in ontogenesis [412, 475, 555].

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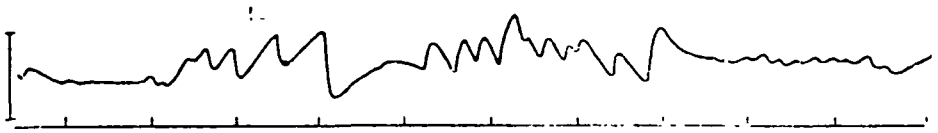

Figure 6. Rotatory nystagmus in man, caused by angular acceleration in the frontal plane (sinusoidal rotation) when the head tilts forward.

Recorded using polarized light (cf. figure 24 and [57, 125].

The basic mechanisms of nystagmus amount to the following. Eyeball oscillations are concomitant and consist of rhythmic alternation of slow and fast version of the eye (components of nystagmus) in opposite directions. Nystagmus always begins with the slow component (SC). This may be literally true, but it would require special procedures during recording of vestibular per-rotatory [580] and reverse post-optokinetic [81] nystagmi to make sure that these reactions begin with SC. The plane of the most intense component of movement coincides with the plane in which angular acceleration acts, because the nystagmus may be primarily horizontal, primarily vertical, or primarily rotatory [378]. The combination of horizontal and vertical movements produces so-called diagonal nystagmus. Rotatory nystagmus consists of wheel-shaped movements -- the eye turns around the optic axis. Sometimes this nystagmus is called torsional. In man it appears during version in the frontal plane (cf. figure 6); in rabbits and other animals with laterally positioned eyes, during version in the sagittal plane.

Under natural conditions, VN results from asymmetric change in afferent flows from symmetric semicircular canal receptors. The greater the asymmetry, the more sharply pronounced the nystagmic reaction. Angular acceleration causes asymmetry in afferent flows under normal conditions. It acts on both labyrinths simultaneously in such a way that the change in afferentation is in different directions -- it increases on one side and decreases on the other. Afferent flow from lateral canal

receptors increases during cupuloendolymphatic shift toward the ampulla (ampullopetal shift of the endolymph or utriculopetal deviation of the cupula) and decreases during shift from the utriculus toward the canal (ampullofugal shift, utriculofugal deviation). In vertical canals, the relationship is reversed: afferent flow increases during utriculofugal cupula deviation and decreases during utriculopetal.

An extensive amount of literature has been devoted to cupuloendolymphatic dynamics. This literature reflects various points of view. For example, for a long time the cupula was conceptualized as an elastic gate [547], similar to a door; but, according to certain data, the cupula is a membrane which surrounds the ampulla[358, 450]. Further, the possibility has not been excluded that both endolymph and perilymph participate when signals develop in the semicircular canal [223, 371, 585]. The physiology of labyrinth system fluids is an extremely important, independent branch of vestibular system physiology, to which a great deal of literature is devoted (cf. for example, the review in [166]). Labyrinth biophysics and hydrodynamics are also constantly at the center of attention of researchers and, ever since a formula for cupuloendolymphatic shift was first proposed [547], these problems have frequently been subjected to testing and clarifications [50-55, 73, 75, 77, 82, 84, 339, 492]. Regardless of the importance of the information in and of itself, it still does not change our basic understanding of nystagmus and its mechanisms. Therefore, the traditional terms "endolymph shift" and "cupula deviation" are used here. /20

Semicircular canals form three functional pairs. In each pair, intensification of the afferent impulse from the receptors of one canal is accompanied by simultaneous weakening of the flow of impulses from the other. If rotation in the horizontal plane is accelerated to the right, for example, signals from the right lateral canal (canalis semicircularis lateralis dextra) predominate, and horizontal nystagmus with a fast component (FC) occurs to the right. If this rotation slows, signals from the receptors of the left lateral canal (canalis semicircularis lateralis sinistra) become predominant, and horizontal nystagmus is directed to the left. If the head turns in the plane of a functional pair of vertical canals in a human, diagonal nystagmus occurs. If, for example, there is accelerated version forward and to the right in the plane of a functional pair formed by the right upper canal (canalis semicircularis superior dextra) and by the left lower (canalis semicircularis inferior sinistra), then afferent flow from receptors in the upper right ampulla will predominate (utriculofugal diversion of the head). Nystagmus in this case will be along the diagonal from the top left downward to the right. (It is accepted to identify nystagmus direction along the FC in the head's coordinate system.) In all cases, SC direction coincides with the direction of endolymph shift. The principles are preserved

even when asymmetry develops due to an increase (or decrease) in only one afferent flow (fistular symptom, elimination of function of one labyrinth, caloric test). A caloric test makes the dependence of nystagmus direction on the direction of endolymph shift particularly clear. If the head is in a fixed position, we can produce nystagmus to the right or left by stimulating one labyrinth (e.g. the right) by heating or cooling. Use of just one type of stimulation (heating or cooling) and changing only the orientation of the labyrinth in the gravitational field by turning the head (e.g. around the bitemporal axis), can also produce nystagmus in two directions, i.e. toward both the stimulated labyrinth and the untreated labyrinth [410, 453]. Thus, caloric nystagmus in any direction can be produced by combining two factors: temperature and head position. Nystagmus can also develop even without the endolymph, when a change in the level of activity (suppression or excitation of one labyrinth) occurs, for example, as a result of an inflammatory process. Under these conditions nystagmus is directed toward the labyrinth whose level of afferentation is higher. Several researchers [17, 32-34, 232, 304, 360, 361] have participated in discovering the basic principles of nystagmus. The most important properties of nystagmus were named "Ewald's principles" in recognition of this natural scientist's service (cf. [379]). /21

Later, as more research was done with new procedures, these laws were subjected to testing and clarification. Ewald's second law in particular was reconsidered and, as a result of continued discussion (cf. e.g. [228, 231, 292, 331, 343, 365, 454], the concept was clarified relative to "effective" and "ineffective" endolymph currents. It was shown that the law of nonuniform stimulus effectiveness is valid for high-intensity stimuli and that there is a range of minor stimuli within which cupuloendolymphatic shifts in the opposite direction cause symmetric responses, i.e. identical in absolute value and different only in sign.

Our understanding of the mechanisms by which vestibular nystagmus develops is becoming more detailed as research procedures are refined and new facts are discovered[178]. In particular, it has been shown that, in addition to nystagmus in the plane of rotation (quantitatively preponderant), nystagmic eye movements occur in other planes[133, 134, 187]. This indicates that canals interact. Since this fact may be of interest in the growth of applied research, it will be dealt with in more detail.

Nystagmus as a Reaction Reflecting Interaction Among Semicircular Canals

Data on the interaction among semicircular canals is scarce. Information that rotation in a horizontal plane stimulates receptors in not only the horizontal, but also the

vertical canals was first obtained during electrophysiological experiments on cold-blooded animals. At first the effect of stimulating semicircular canals lying outside the plane of rotation was observed in a classic study by Lowenstein and Zand [434]. The subject was an isolated preparation of a skate labyrinth; the stimulus: angular acceleration. The electrical activity of the branches of the ampullar nerves was recorded. In particular, this research established that all four vertical canals react to a stimulus addressed to the horizontal canals. If rotation counterclockwise around the vertical axis is accelerated, receptors of the right anterior and left posterior canals are excited, while receptors in the left anterior and right posterior canals are inhibited. If the sign of the acceleration changes, excitation is replaced by inhibition and inhibition by excitation. /22

In a study on a frog [84], the electrical activity of identical nerve pili of anterior and lateral ampullae was analyzed during local caloric stimulation of the lateral canal. It was observed that utriculopetal shift of the horizontal canal endolymph (warm test) is accompanied by an increase in afferent pulsing in the nerves of not only the horizontal, but also the vertical ampulla. It was concluded that this effect underlies the hydrodynamic interaction among semicircular canals.

Important results were obtained in experiments also done on frogs, but under the condition that efferent effects on the labyrinth were entirely eliminated [262]. The stimulus was angular acceleration. The following was concluded: during utricular shift in the horizontal canal, changes in activity in the afferent pili of this canal and of the anterior vertical canal of the same labyrinth are opposite in sign. Thus, it was shown that the effect depends neither on efferent influences, nor on direct nerve links among canal receptors.

Laurente de Nó showed that all six extraocular eye muscles in a rabbit react to stimulation by rotating in the plane of any pair of semicircular canals. An even more complex picture develops when both canals and otolithic organs are subjected to stimulation [427]. This data was obtained during an opthalmectomy and can provide no understanding of eye movement under natural conditions.

Studies begun by Laurent de Nó were expanded in work by Szentágothai [552] devoted to discovering the specific, governing relationship between each receptor and the extraocular muscles -- direct reflector arcs along which tonic reflexes occur. Critical experiments on cats and dogs involved recording and measuring contractions isolated by muscle enucleation in response to mechanical stimulation of labyrinth receptors. In particular, it was shown that the plane of eye movement during the action of a vestibular stimulus on identical receptors depends on the type of animal -- more precisely, on

the location of the eye relative to the cranium. For example, /23
utriculofugal endolymph shift in the superior semicircular canal causes the eye of an animal with frontal eye arrangement (cat) to turn upward in the sagittal plane, but in an animal with lateral eye arrangement (dog), it causes a wheel-like turn downward in the sagittal plane. Given simultaneous stimulation of several receptors, the ultimate result of the vestibulomotor reflex, i.e. complex eye movement, is the simple sum of basic, typical reflexes from stimulated receptors.[1] This conclusion is important since it justifies considering not only tonic reflexes, but also complex forms of nystagmus, as sums of simple ones. For example, we can hypothesize that horizontal-rotatory nystagmus is the result of adding horizontal nystagmus whose origin is related to lateral canal receptors, and rotatory nystagmus caused by stimulation of vertical canal receptors.

This hypothesis led to a study on rabbits in which nystagmus caused by angular acceleration was recorded cinematographically [133, 134, 137]. Rotation was in the horizontal plane and was accomplished according to a trapezoidal program (positive acceleration $10^{\circ}\cdot sec^{-2}$, velocity $166^{\circ}\cdot sec^{-1}$ over 120 seconds; negative acceleration $10^{\circ}\cdot sec^{-2}$). The animal's head was fixed to ensure that the plane of the lateral semicircular canals coincided with the plane of rotation, while the axis of rotation ran between its ears. (In part of the experiment, rotation was accomplished with eccentricity, i.e. centrifugal force equivalent to 0.5 g was added.) Filming made it possible to record eye movements regardless of their complexity and subsequent frame-by-frame evaluation of coordinates (cf. figure 7) allowed the components of this movement to be calculated and presented separately for each of the three planes in the form of a continuous path-time chart. The procedure's accuracy, at least equal to that achieved during photonystagmography [109, 140], ensured that amplitude characteristics with an error no greater than-2% were obtained. The multiplanar nature of the vestibular reaction was observed in all experiments. In no case was nystagmus horizontal in the strict sense of the word. Version around the vertical axis (horizontal nystagmus, or the horizontal component of nystagmus) took place around the naso-occipital axis (the vertical component), and also around the bilateral axis -- more precisely, around the optic axis of the eye in the sagittal plane (the rotatory component). It has been established that each component of the oculomotive reaction has three elements: 1) a rhythmic element, or nystagmic oscillations, a necessary indication of which is regular alternation of slow and fast components forming /24
nystagmic pulses; 2) a tonic element, or elapse, which allows

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1 The possibility of adding reflexes caused by simultaneous electrical stimulation of two anterior canals has also been demonstrated in other works (cf. for example, [550]).

nystagmic pulses to occur not around the initial position, but with a more or less significant shift toward the slow or fast component; 3) a tonic element of otolithic origin, regularly appearing only if there is eccentricity and related this eccentricity by centrifugal force. All three elements in each component can be identified only by artificial techniques. In natural conditions all of them participate simultaneously to form an eye movement.

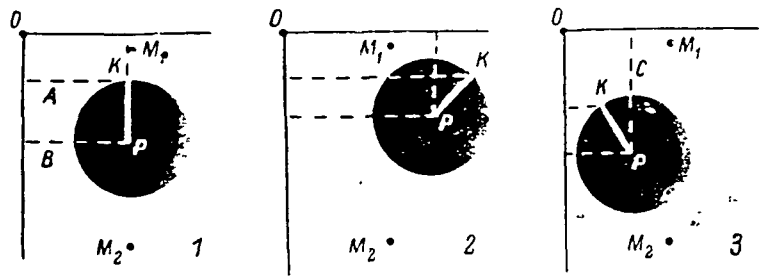

Figure 7. Principle of frame-by-frame evaluation of a filmed nystagmogram of the right eye of a rabbit to identify horizontal, vertical, and rotatory components of movement.

The position of marks (M_1 and M_2) applied to branches of the blepharostat and fixed in cranial coordinates are noted on a screen equipped with a coordinate grid during projection of the first frame (0 - origin). PK - projection on the screen of an image of the radius-marker fixed on the eyeball. Sections A, B, and C correspond to three measurements taken in sequence on each frame. The representative frames show: (1) neutral position of the eye; (2) a combination of diversion downward and version in the nasal direction around the vertical axis, clockwise around the optic axis, and upward around the naso-occipital axis; (3) a combination of deviation downward, turning in the occipital direction in the horizontal plane, and rotation counterclockwise. Section B gives an idea of the extent of horizontal version; section C -- vertical; and the arc-sine of the ratio of the difference in sections A and B to the projection of the radius-marker PK -- rotatory.

The most pronounced of the three components (in terms of rhythmic element amplitude) is horizontal; the least pronounced is vertical (cf. figure 8). The rotatory component occupies an intermediate position. It is less pronounced than horizontal, but fully commensurate with it, while its amplitude is 25 to 50% that of the horizontal.

In most cases, rhythmic elements of various components have

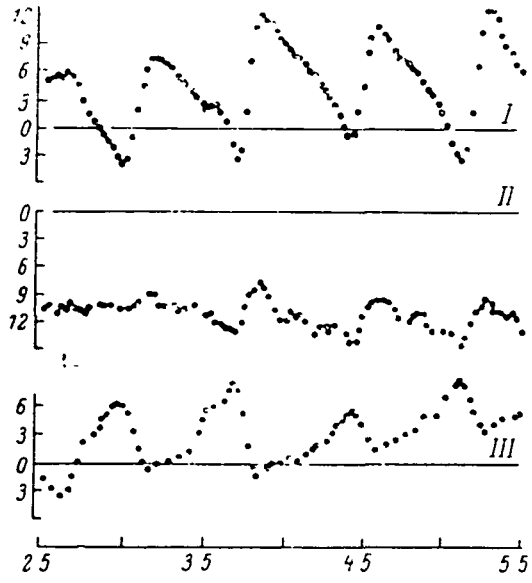

Figure 8. Reconstruction of three components of nystagmus in a rabbit from a fragment of a filmed nystagmogram of the right eye (as per [133]).

When the animal turns to the right in the plane of the lateral semicircular canal, positive angular acceleration produces complex movement, including (I) horizontal nystagmus to the right, (II) vertical nystagmus upward, and (III) rotatory nystagmus counterclockwise. A tonic element occurs in each component. X-axis -- time from onset of acceleration, sec; Y-axis -- turns of the eyeball (zero corresponds to a position at rest).

identical frequency and are synphasic (i.e. nystagmic pulses in all three planes occur simultaneously [cf. figure 9]). However there are exceptions: when rhythmic element frequencies in various components do not match.[1] For example, it turned out that the frequency of rotatory nystagmus can be double that of horizontal.

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1 There is data indicating the presence of independent paths and centers, which ensure nystagmus in various planes. For example, one publication[311] presents electronystagmograms (ENG's) which simultaneously recorded eye movements in a human in horizontal and sagittal planes. It was shown that horizontal and vertical nystagmi have different frequencies. This makes it possible draw conclusions about their formation in different centers.

If the direction of test stand rotation is unchanged, the direction of rotatory nystagmus (i.e. of the rhythmic element of eye version in the sagittal plane) depends on the sign of angular acceleration. If it turns to the left, for example, positive angular acceleration causes rotatory nystagmus, the FC of which is directed clockwise, while negative angular acceleration causes nystagmus with a counterclockwise FC.

The mechanism by which the rotatory component of nystagmus arises during a horizontal rotatory test can be represented as follows. Angular acceleration, acting on a labyringh in the plane of lateral semicircular canals, causes cupuloendolymphatic shift in all vertical canals. These shifts apparently are subject to a rule which can be formulated thus for one labyrinth: shifts in anterior and lateral canals are similar, but those in posterior canals are opposite. For example, in accelerated rotation leftward (cf. figure 10), utriculofugal currents arise in the right lateral and right anterior vertical /27
canals; utriculopetal current arises in the right posterior vertical canal. The mnemonic rule can be devised thus: from a common reservoir (vestibule), endolymph flows along two paths: anterior and lateral canals; it flows to the posterior canal from the anterior. This understanding of the cupuloendolymphatic shifts (table 1) which cause the rotatory component correlates well, first, with the results of electrophysiological experiments [434] and, second, with data obtained using models [56, 163, 167, 171].

Experiments on a physical model of a human labyrinth [163, 165], constructed on the principle of dynamic similarity, have shown that acceleration acting on the plane of the lateral semicircular canals causes cupuloendolymphatic shifts even in vertical canals and that the magnitude of the shift in the anterior canal is greater than in the posterior. In the model [165] anatomical data on the lack in a human of a right angle between the planes of the lateral and anterior canals [246] was disregarded: the angle was 90°. Consequently, first, the right angle between the planes of the lateral and anterior canals did not hinder shifts in the latter and, second, there was no need for the plane of the canal to deviate whatsoever from the vertical plane for shifts to occur.

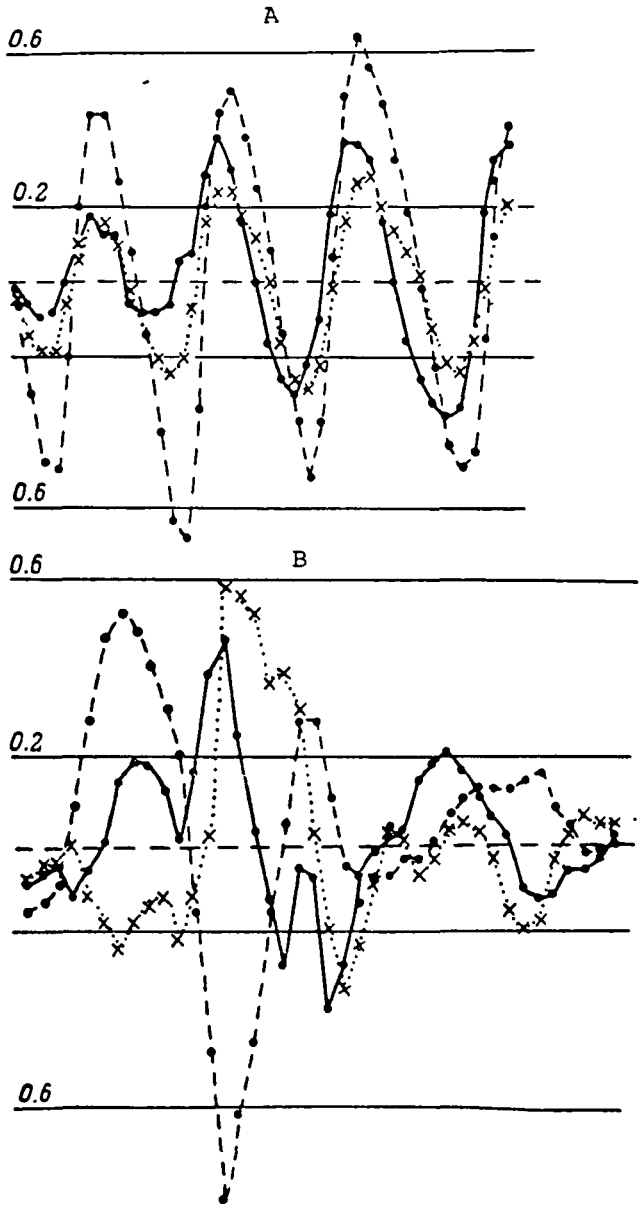

Figure 9. Reconstruction of the three components of eye movement -- horizontal (broken line), vertical (dotted line), and rotatory (solid line) from results of processing two fragments of cinematic nystagmograms [134].

A -- during positive angular acceleration in the exterior semicircular canal plane; B - during negative acceleration. X-axis -- points are at 0.5 sec intervals; Y-axis -- amplitude of versions, normalized according to maximum slow component amplitude (ASC) of the horizontal component. During mathematical processing, in contrast to figure 8, the constant components (tonic elements of eye movement were excluded in each plane).

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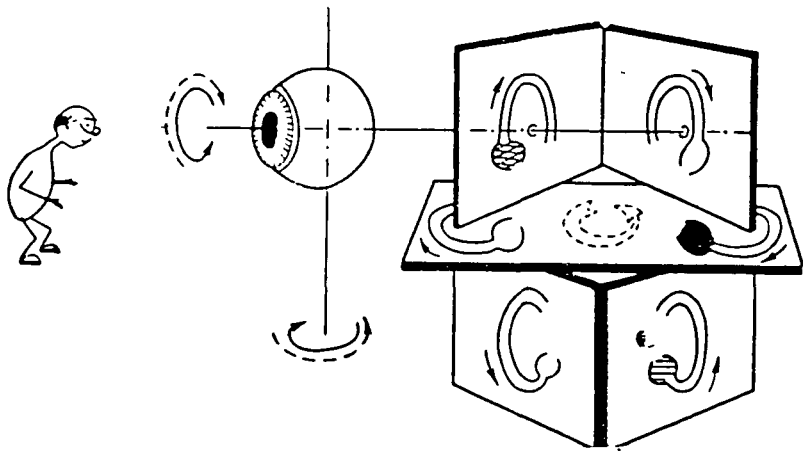


Figure 10. Direction of two components of vestibulo-oculomotor reflex in a rabbit during accelerated leftward rotation in the plane of the lateral canals -- nystagmus in a horizontal plane (eye turns around the vertical axis) and nystagmus in a sagittal plane (turns around the optic axis) [134].

From the observer's standpoint, rotatory nystagmus is directed clockwise (FC is indicated by dotted arrows). Arrows in the semicircular canals show the directions of cupuloendolymphatic shifts. The differing levels of ampullar receptor activity are reflected by the density of the dots.

All this data indicates the actual feasibility of using nystagmometry to study the interaction of labyrinth receptors. /28

TABLE 1. STATUS OF AMPULLAR RECEPTORS AND DIRECTION OF CUPULOENDOLYMPHATIC SHIFTS DURING ACCELERATION AND INHIBITION OF COUNTERCLOCKWISE ROTATION IN A RABBIT IN THE PLANE OF THE LATERAL SEMICIRCULAR CANALS [134]

Rotation	Semicircular Canal	Status	Direction
Accelerated	Right lateral	Inhibition	Utriculofugal
	Left lateral	Excitation	Utriculopetal
	Right anterior	"	Utriculofugal
	Left anterior	Inhibition	Utriculopetal
	Right posterior	"	"
	Left posterior	Excitation	Utriculofugal
	Right lateral	Excitation	Utriculopetal
	Left lateral	Inhibition	Utriculofugal

Table 1 (cont.)

Rotation	Semicircular Canal	Status	Direction
Inhibited	Right anterior	"	Utriculopetal
	Left anterior	Excitation	Utriculofugal
	Right posterior	"	"
	Left posterior	Inhibition	Utriculopetal

The technique of calculating components in a vestibular reflex whose origins can be related to participation of specific receptor formations shows promise even in applied research. On the one hand, it is becoming practicable to obtain additional information about the status of vertical canals in tests with horizontal rotation (possibly even in caloric). On the other hand, the rotatory component even in spontaneous nystagmi may be of interest in diagnosis. The difficulties of studying the rotatory component, arising from the large amount of time required for research, have been eliminated with the development of a simple, interference-proof procedure for recording eye movements [125, 135].

Paths and Centers of Nystagmus. Fast Component Mechanisms

As a result of several studies, the minimum number of nerve structures required to accomplish both phases of vestibular nystagmus has been defined: afferent pili from the labyrinth, efferent pili to the extraocular muscles, and the parts of the central nervous system between afferent and efferent paths [542].

Primarily superior and medial vestibular nuclei take part in vestibular reflexes. There is information on localization of functions in the vestibular nuclei: the anterior part of the nucleus plays the greatest role in vertical eye movement; the posterior in rotatory; the intermediate in horizontal. The medial nucleus is connected to the exterior rectus ocular muscle on the same side and with the interior rectus muscle on the opposite side. The superior nucleus is connected to the interior rectus muscle on the same side and, possibly, to the exterior rectus muscle on the opposite side. These paths may provide tonic vestibulo-ocular reflexes and the nystagmic slow component [269]. /29

It has been established that it is precisely in the superior and medial nuclei which receive signals from semicircular canal afferents that the greatest number of commissural neurons, which ensure connection among nuclei on both sides, is concentrated [321]. Many morphological and morphophysiological studies have been devoted to connections among vestibular nuclei

[254, 452, 512]. In particular, it has been shown that in an ape, the most extensive connections are those which ensure horizontal and rotatory eye movement [452].

Analysis of a large amount of literature and data from his own experiments allowed S. N. Khechinashvili [195] to conclude that contraction of eye muscles both during labyrinth tonic reflexes and during the slow component of nystagmus results from activation of the same short three-neuron reflector arcs. Later on, electrophysiological studies dealt with a precise clarification of short paths [299]. A large amount of work, beginning with the classic studies of Laurente de Nó [428] has been devoted to studying paths along which vestibulo-oculomotor reflexes occur, as well as centers which take part in these reflexes. One recent study in this group is a monograph on the morphology of connectors in the cortical vestibular zon e[66]. Information which makes it possible to relate morphology to function and specific properties of nystagmus to a particular structure are of the greatest interest from the standpoint of applied nystagmometry. There is great controversy in published literature on FC mechanisms. For a long time, the role of proprioceptive afferentation from extraocular muscles in the formation of nystagmic rhythm and FC was a topic of discussion. There is now adequate justification not to attribute a leading role in nystagmic rhythm to muscular proprioception [192, 399, 418, 448, 449, 511].

Let us focus on one study [449]. Nerve branches to the interior muscles of both eyes of a cat, except for the abducent nerve (which innervates one of the exterior rectus muscles, had been severed beforehand). Under light ether anesthesia, a caloric test caused rhythmic change which corresponded to nystagmus phases and direction in the electrical activity of the untreated nerve. After the latter nerve was separated from the muscle, the activity in it changed, as before, to the rhythm of nystagmus. In other words, FC took place in conditions which completely eliminate involvement of muscular proprioception.

A study of the interaction of two afferent flows from the vestibular apparatus and from extraocular eye muscle extension receptors showed that the electrical activity of cells of the reticular formation (RF) of the truncus cerebri is somewhat affected by muscular proprioception, just as in vestibular nuclei and longitudinal fascicles. Most important, this effect was not observed in the motor nuclei of the extraocular muscles. The role of these proprioceptive influences is not clear. They apparently have no direct relationship with nystagmus [323]. /30

We can also probably reject the hypothesis of the cortical origin of the FC also, since facts show that the reflector arc of a nystagmus is closed past the cortex (cf. review: [2]). Experiments on cats[65] showed that mild anesthesia, freezing the cortex with chlorethylene, and decortication of the

anterior, temporal, and parietal parts of the brain not only do not curtail nystagmus, but even prolong the reaction somewhat. According to K. L. Chilov [196], these facts indicate the inhibiting action of the brain cortex on vestibulosomatic reflexes.

The work of Laurente de Nó has played a significant role in investigating the origin of nystagmic rhythm, especially in the origin of the fast component. His work resulted in the discovery that the SC and the FC of nystagmus in a rabbit are related to different parts of the central nervous system[429]. In particular, cuts made in a rabbit above the reticular formation of the pons eliminated the FC. Similar experiments on cats [538, 541] produced the same effect. The idea has developed that primary vestibular nuclei send a continuous flow of pulses which, at some relay, are transformed into rhythmic alternation of excitation and inhibition, which determines the contraction and weakening of eye muscles typical of nystagmus. Since primary vestibular nuclei have no cell system connected directly to eye muscles, the reticular formation (RF) must be considered the key to the development of nystagmic rhythm. The effect of various parts of mesencephalic RF on nystagmic rhythm was shown especially in experiments involving simultaneous electrical stimulation of the lateral vestibular nucleus and RF: horizontal nystagmus, caused by nucleus stimulation, can be modulated (enhanced or diminished), depending on the location of the electrode in the RF [590].

McCabe [446] dealt with the role of the RF in the development of nystagmus and its rhythm, i.e. the origin of the fast component. Experiments on cats with various combinations of vestibular nucleus coagulation, specific pharmacological action on the RF, and electrolytic damage to the RF close to the nuclei were accompanied by careful quantitative analysis of the FC and SC of the nystagmus. Changes in each component were evaluated in terms of rate of eye movement. This study conclusively proved the autonomy of the vestibular nystagmus FC system and /31
the significance of the RF's role in organizing nystagmus. Comparing the results of his experiments with observations of other researchers on the mechanisms by which nystagmus and its FC form, McCabe proposed a rather strict, simple plan which amounts to the following. Nerve paths reaching the nuclei of extraocular muscles through the RF and through the medial longitudinal fascicle take part in vestibular nystagmus. The reticular formation is responsible for the FC (possibly separate from the SC), while the medial longitudinal fascicle serves as the main path of the slow component. From here impulses along pili, passing in the medial longitudinal fascicle and the RF, enter the nuclei of the extraocular muscle and cause the SC of the nystagmus. In addition, impulses also reach the activating neurons of the RF, which have a certain threshold. If the impulses exceed this threshold, these neurons trigger, performing two functions simultaneously: first they activate the

mechanism which brings about FC; second, they trigger inhibiting neurons. The latter in turn interrupt the flow of impulses involved in SC formation. Thus, nystagmus is caused by coordinated interaction of neurons in the vestibular nuclei and RF neurons. RF neurons provide the dynamic combination of volleys of impulses responsible for FC and inhibit SC. Although we still cannot assert that RF neurons are a source of FC, there is no doubt about their effect on the rhythms of vestibular nystagmus, and consequently on FC formation. McCabe's model is simple and, for this reason, very attractive. At the same time, we cannot ignore the fact that the development of nystagmic rhythms is complex. Changes in neuron electrical activity in a rhythm typical for nystagmus were observed in the vestibular nuclei themselves [298], in the RF of the hindbrain, and in intermediate neurons of the abducent nerve nucleus [370]. The reticular formation of the truncus cerebri of a cat exhibited inhibited neurons whose activity directly correlated with the participation of nuclear motoneurons in the fast phase of nystagmus [357]. These concepts are much more complex. The dorsomedial parts of the truncus RF exhibit neurons which inhibit motoneurons of the abducent nerve contralateral nucleus in the pauses between slow components of homolateral nystagmus. In contralateral nystagmus these neurons are quiescent [356]. The rhythm of vestibular nystagmus is also apparently defined by nerve structures localized in the posterior parts of the medulla oblongata [299, 300]. It has been shown that Darshkevich's nucleus is involved in the mechanism of nystagmus. Stimulating it weakens contracted muscles and inhibits nystagmus [532, 553]. There is also data on the inhibiting effect of Cajal's nucleus on vestibular nuclei [441]. Integration of the sensory (vestibular or optic) inlet and the oculomotor (nystagmic) outlet occurs in extensive areas of the brain [237]. A multitude of facts similar to these await even more detailed analysis and generalization. /32

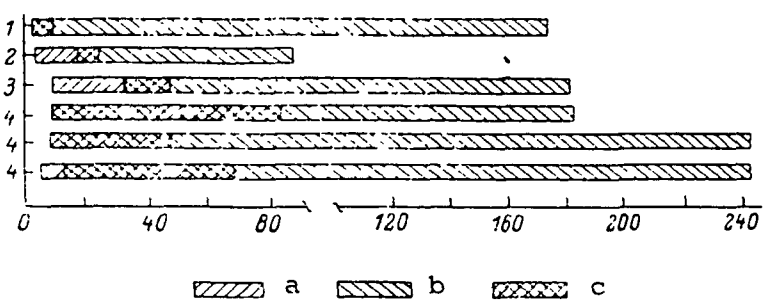


Figure 11. Overlap of SSC (slow component speed) and SFC (fast component speed) of post-rotatory nystagmus in a rabbit (from [111]).

X-axis -- angular velocity at which the eye turns around the vertical axis, $^{\circ}\cdot sec^{-1}$. Y-axis -- rabbit number; a -- SSC; b - SFC; c -- overlap zone.

Although block diagram details and the paths and centers taking part in achieving nystagmus are at present complex and important, there is another approach at least as interesting and promising. It is based on careful quantitative study of the reaction itself, i.e. nystagmus. For example, to identify FC mechanisms, it is useful to evaluate FC speed. This characteristic is useful because there is a great deal of data on its relationship to the other (slow) component: its relationship to stimulus intensity, the nature of change over time and several others. There is also data on tonic reflex speed: maximum speed of tonic contraction of the eye muscle is a linear function of the logarithm of the frequency of the electrical stimulation of the ampullar nerve, i.e there is a direct proportional relationship between speed and stimulus [549]. /33

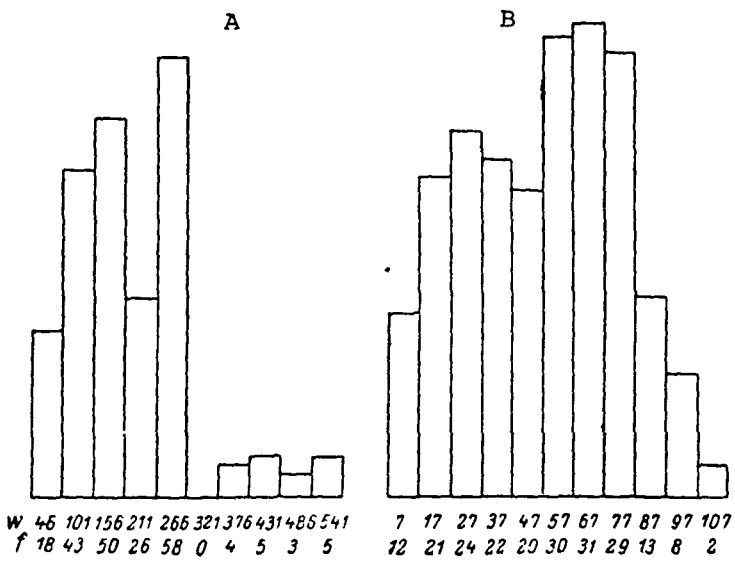


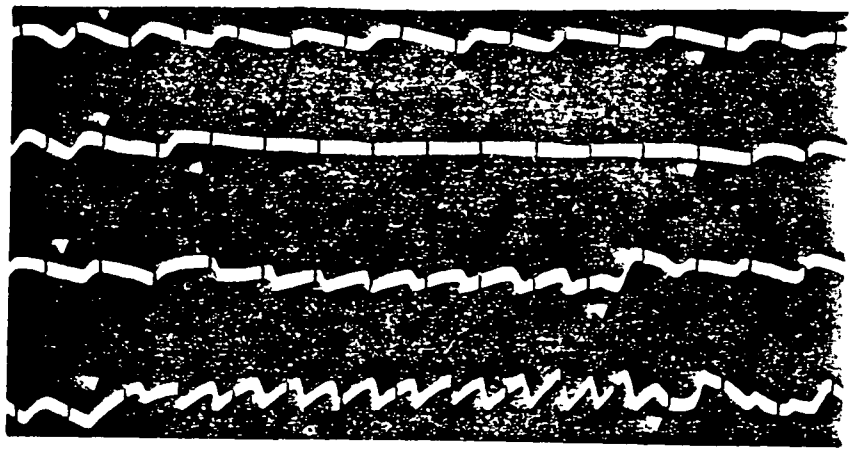
Figure 12. Histograms of (A) SFC and (B) SSC of post-nystagmus during Barany's test on one rabbit

Data from 7 post-rotatory nystagmograms on one animal (212 nystagmic impulses). W -- the middle of the class, f -- the number of impulses.

Eye movement speed in a particular phase is a characteristic which can serve as the basis for comparing the function of the FC and SC systems. When SC and FC speeds are measured consecutively at each nystagmic impulse caused by angular acceleration, a rabbit exhibits an SFC which varies over such a wide range (cf. figures 11 and 12) that the lower variation boundary overlaps the SSC's upper variation boundary throughout the entire reaction. This fact is interesting from the standpoint of applied nystagmometry. It shows that the absolute value of eye movement speed in any nystagmogram fragment cannot be reliable enough evidence to distinguish SC from FC. A particular fragment can be classified only by comparing it with the adjacent section of the record. Physiological experiments on rabbits [109] and on cats [338] established that SFC and SSC are not directly dependent on one another. One publication [402] states that human nystagmograms can exhibit a positive correlation between SFC and SSC. Local electrical impulse stimulation of the ampullar receptor apparatus of one lateral canal in a

rabbit [110, 112, 113] revealed that SFC and SSC are a function of impulse frequency (cf. figures 13 and 14). It turned out that FC is regulated according to the level of vestibular afferentation. However, the relationship of SFC to stimulation frequency is quite different from that of SSC. This data correlates well with data on changes in SFC and SSC during angular acceleration [109, 422]. Thus, there is sufficient justification to assert that two systems are involved in the nystagmic reflex: the SC system and the FC system. Identical afferentation from the ampullar apparatus traveling through the system of vestibular nuclei arrives at the same time at both systems. These two systems are relatively independent, not only morphologically, but functionally as well. The FC system converts a continuous (tonic) reflex into rhythmic reflex (nystagmus), fragmenting the tonic reflex into the slow components of consecutive nystagmic impulses and causing abrupt movements (FC) between slow components. Tonic reflex fragmentation

A



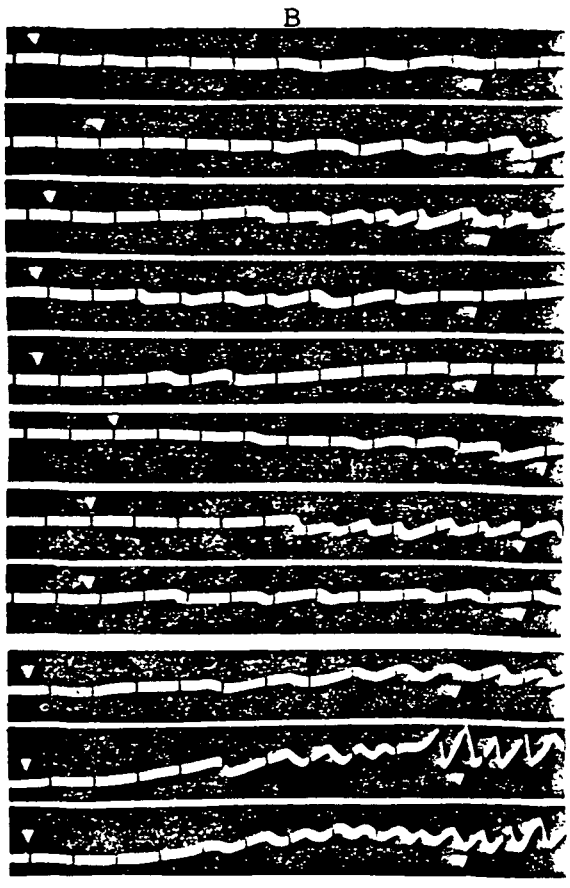


Figure 13. Horizontal nystagmus in a rabbit during rhythmic electrical stimulation of ampullar receptors by a series of rectangular impulses lasting 0.2 msec (from [111]).

Photonystagmograms (cf. figure 17 and [104, 108]) of the left eye during stimulation of the right labyrinth. A shows records of one experiment. Stimulation during downward nystagmus, direction toward the untreated (right) labyrinth. The beginning and end of stimulation are indicated by triangles. Nystagmograms are recorded at the following stimulation frequencies (from the top down): 30, 50, 70, and 90 Hz. It is apparent that the effect depends on stimulation frequency: at 50 Hz, full inhibition of the descending nystagmus occurred, but at 70 Hz the reverse took place. B shows records in three experiments. The symbols have the same meaning as in A. Frequencies: in the first experiment -- 10, 20, 30, 40, and 50 Hz; in the second -- 10, 30, 50 Hz; in the third -- 20, 40, and 60 Hz (optimum frequencies which cause the highest SFC are underlined.

and SFC adjustment are a function of the level of impulses from receptors (cf. figure 15), but the FC system is tuned to a certain afferent impulse frequency [107, 110, 112-114]. That these two systems participate in the development of nystagmus is indirectly confirmed by the fact that the oculomotor apparatus of mammals, i.e. the efferent network of vestibulo-oculomotor reflexes, exhibits two systems distinguished in terms of electromyographic characteristics: fast (phase) and slow (tonic) [12, 143, 145]. It is quite probable that the idea of two systems is somewhat simplified; in fact there are other systems which adjust, for example, the transition from SC to FC, from fast movement to slow, etc. [200-203]. Our understanding of the mechanisms by which nystagmus develops has been considerably enriched after a study of the electrical activity of individual muscle elements -- eye muscle motor units in a rabbit with optokinetic nystagmus [151, 203]. In particular, it has been shown that the duration of the SC is somehow predetermined from its very onset (which again justifies the idea of the vital role of muscular proprioception in regulating nystagmic reaction). The idea that active inhibition of the abrupt change is programmed has also been confirmed [206]. It has been observed that motor units are functionally mobile and that the same unit can take part in both SC and FC, depending on the direction of the nystagmus [202].

The mechanism by which nystagmus SC and FC are organized cannot be considered contradictory to data on eye movement physiology. From this standpoint, the SC of vestibular nystagmus is a particular case among abrupt eye movements. A great deal of information has been acquired about these movements. For example, the mechanics of saccadic eye movements in a human [520] have been studied. Facts indicate that muscle proprioceptors have no significant role in organizing an abrupt change [522], and the change program (amplitude, duration, speed) is already formulated before movement begins [141, 142]. If FC is considered to be the result of activity of the same mechanisms which are responsible for saccada[523], we can conclude that the FC program is formulated regardless of SC amplitude: this program either exists by the time the nystagmic impulse begins or builds up as the SC is taking place, but its development is /36
finished before the SC is completed. Speaking of SC and FC mechanisms, we cannot help but mention that the density of the nystagmus must be taken into account in each specific instance. For example, the opinion has been expressed that slow components of horizontal and vertical nystagmus are controlled by separate, independent centers, while FC centers for these nystagmi are shared [311].

The problem of FC mechanisms is directly related to applied nystagmometry. The relative autonomy of the two systems which bring about nystagmus indicates the need, on the one hand, for a critical approach to selecting nystagmometric characteristics by which nystagmus must be evaluated in vestibulometric

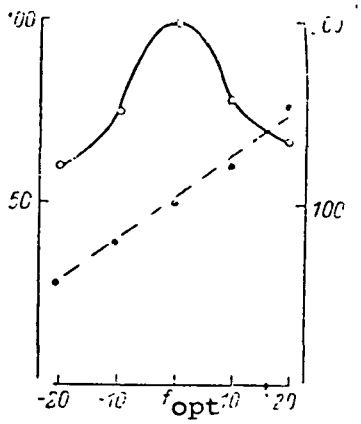


Figure 14. SFC (solid line) and SSC (broken line) as a function of frequency of rhythmic electrical stimulation of the ampullar receptor (from [111]. /36

X-axis -- optimum (f_{opt}) and adjacent frequencies within ±20 Hz; Y-axis -- SFC (left) and SSC (right), % of value obtained at optimum stimulation frequency.

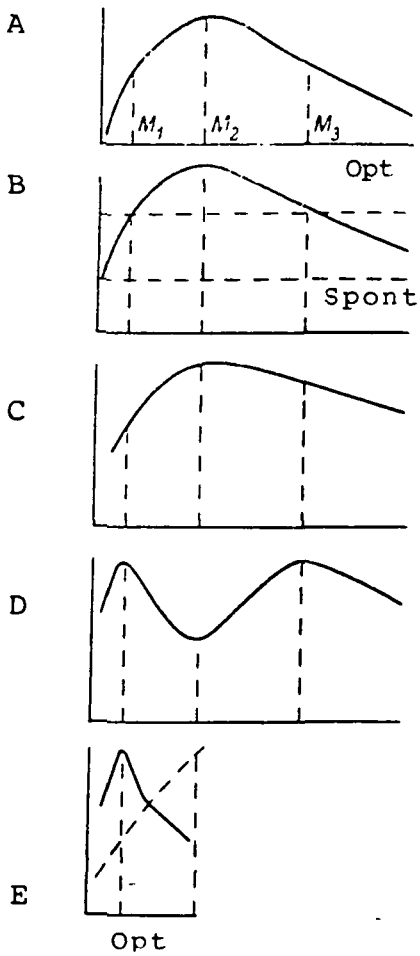


Figure 15. Role of ampullar afferentation in formation of the FC of nystagmus (from [111]).

Ampullar hypothesis in graph form. Comparing the reaction at stop-stimulus (A-D) and the results of local electrical stimulation of the ampullar receptor (E). X-axis on A-D -- time; on E -- electrical stimulation frequency; Y-axis: on A -- cupula deviation at different points after rotation stopped; on B -- afferentation from ampulla receptors varying from spontaneous impulses to maximum; on C -- SSC; on D -- SFC; on E -- SSC (broken line) and SFC (solid line). Scales are conventional. Optimum afferentation frequency occurred twice -- at moments M_1 and M_3.

practice and, on the other hand, for comprehensive evaluation of the reaction, since it determines the actual possibility of obtaining additional information on vestibular function, /37

particularly about injury. Pathological changes in the rhythmic system are apparently possible if the tonic system's function is completely preserved [118]. It follows, then, that in evaluating nystagmic reactions, the choice of parameter used to compare reactions which differ in direction is quite important [138].

Thus, signals from the vestibular apparatus to the extraocular muscle, transmitted in a physiological experiment directly along a three-neuron vestibulo-oculomotor reflector arc, are only a simple mechanism of vestibulo-oculomotor reaction. Under normal conditions, the connection is made by the most complex nerve in the network. To explain these complex relationships, it is useful to construct models based on experimental and clinical data. Models often make use of analogs of technical devices, the concept of a "network," "cascade transmission," "feedback," etc. We should mention, for example, the system for regulating eye motility during tonic vestibulo-oculomotor reflexes [294] based on data from a study of electrical activity of single nerve elements in the vestibular nuclei and the RF. This system accounts for the polysynaptic vestibular path through the reticular formation and the effect of labyrinths on all extraocular muscles. In general, modeling is quite important in studying the vestibular system and its reactions. Chapter 4 covers modeling nystagmic responses to bithermal tests in the norm and in certain pathological conditions, as well as diagnostic use of models.

Weakening of Nystagmus

In the physiology of vestibular nystagmus, there exists a phenomenon known as extinction. Soviet literature uses the literal translation "adaptation," or the term "fading" as an equivalent to "habituation". "Habituation" seems preferable, since it better represents the essence of the phenomenon. Extensive literature [27, 40, 41, 206, 276, 312-315, 368, 369, 424-426, 497] has been devoted to this phenomenon. It can be described as follows: during repeated individual stimulations sufficient to cause nystagmus, the intensity of the reaction (evaluated, for example, in terms of SSC) decreases as the number of stimulations increases. There is also a decrease in nystagmus duration -- more evident as stimulus force increases. The habituation reaction can also be produced with stimuli which vary in magnitude from one to another -- either increasing or diminishing [27]. The habituation of nystagmus has been described in man, apes, cats, rabbits, and pigeons. It is a unique reaction, different from depletion and adaptation, and /38 depends on central mechanisms whose location is still not clear [353], although some feel that the cerebellum is responsible for habituation [424]. Experiments on decorticated cats indicate that this phenomenon occurs in lower centers, possibly in the RF of the medulla oblongata and the pons, as well as in vestibular nuclei [308, 396]. The possibility that efferent

vestibular enervation [447] is involved has not been excluded. The phenomenon does not exist in animals lacking one labyrinth [46].

The most typical features of habituation have been identified -- those which distinguish it from other phenomena also associated with a decrease in reaction: depletion, retention, and transfer. Depletion involves a gradual reduction in the nystagmus intensity from one stimulation to another, subject to a law close to exponential. The last two qualities were the subject of a study on caloric stimulation of cats [309, 336, 353, 459, 460, 498]. Retention occurs when a reduction in nystagmic intensity achieved by repeated individual tests occurs even after a long time (up to 3 weeks). The essence of transfer can be conveniently explained by example. Habituation of leftward nystagmus occurs through the use of cool tests on the right ear, but the nystagmus which results from a warm test on the left ear also fades. In other words, habituation is manifest during nystagmus in one direction, regardless of which labyrinth was stimulated to produce it. The coincidence of planes is important: the intensity of horizontal nystagmus does not decrease if a pair of vertical canals is repeatedly stimulated [282]. Habituation caused by caloric stimulation does not show up in the results of rotatory tests [499]. Information has appeared which indicates that habituation of vestibular nystagmus can cause optokinetic stimulation in apes and that the same regularities which occur during habituation of the response to vestibular stimuli occur in its development [589]. If habituation of nystagmus has developed with the head in a specific position, then, if head orientation changes, nystagmus in the same direction does not exhibit signs of habituation [278]. The subject is exposed to vestibular stimuli in darkness, habituation becomes more noticeable [274], but the involvement of vision in experiments with rotation has no effect on the rate at which habituation develops. It only diminishes the superficial manifestation of the phenomenon [281]. The assumption that habituation can be inhibited by artificially stimulating an animal has not been confirmed [283]. There is information indicating that individual capacities for habituation can be important in diagnosis [290, 366]. Since the phenomenon of fading is formally analogous to the phenomenon of directional preponderance observed in diagnostic research using bithermal testing (BT), the model described in chapter 4 may be useful in studying the mechanism of fading. /39

The Effect of Various Parts of the Central Nervous System on Vestibulo-Oculomotor Reflexes

Vestibulo-oculomotor reactions are subject to corticofugal, cerebellar, somatosensory, and other effects. Vestibular function is controlled by the cortex of the brain [196]. However, the problem of cortical influences is quite complicated. Evidence of the existence of direct corticofugal pili leading to

vestibular nuclei is still inadequate and often contradictory [66, 254]. One study [99] has established that pili beginning in the cortical vestibular zone of a cat reach the nuclei of the vestibular complex of the medulla oblongata (ipsi- and contralateral) without interruption. These morphological findings shed light on facts from electrophysiological research on changes in vestibular nuclei activity during cortex stimulation, since they conclusively demonstrate the possibility of efferent controlling actions along monosynaptic paths. Corticofugal impulses control various forms of nystagmus [301, 203, 587]: spontaneous after a unilateral labyrinthectomy, compensatory [540], caloric, and optokinetic [261, 310]. At the same time, it has been observed that decortication has no major impact on the capacity of the vestibular apparatus to evaluate the magnitude of a stimulus. For example, it has been shown that the relationship between nystagmus duration and stimulus strength is preserved after decortication in pigeons [191] and in rabbits [26].

The close anatomical and functional relationship which exists between the vestibular system and the cerebellum [284, 345, 374, 394, 407, 476] is also of interest from the standpoint of applied nystagmometry. For example, experiments on chinchillas [284] demonstrated that the flocculus takes part in the interaction of the vestibular and ocular systems: the quantitative characteristics of compensatory eye movements which occur during head oscillations and usually depend on participation of vision after a bilateral flocculectomy become independent of visual fixation. The presence of inhibitive control of oculo-vestibular paths from the cerebellum has also been demonstrated in experiments on rabbits [411]. Somatosensory information plays a minor role in mechanisms of vestibulo-oculomotor reactions [525].

So-called extra-labyrinthine factors are significant in the physiology of nystagmus. These are nonspecific effects which have a modulating action on various levels of nystagmic mechanisms and ultimately on the quantitative characteristics /40
of nystagmus. The term "extra-labyrinthine factors" is used rather broadly and inconsistently. For example, it is used to identify individual features of the subject which promote strengthening (or fading) of the effect of caloric stimulus (a defect in the tympanic membrane, individual anatomic peculiarities of the structure of the acoustic meatus and mastoid process). Of no less interest are extra-labyrinthine factors of another type, namely the action of stimuli on other sensory systems (vision, hearing, touch, smell) simultaneous with vestibular stimulus. From the standpoint of physiology, studies conducted under conditions when the activity of various systems in an organism is directed toward solving a common problem (cf. e.g. [13]) relate to the broad problem of the interaction of sensory systems. The study of the interaction of vestibular and auditory systems in particular is interesting and multi-

faceted. Here are just a few of its aspects. Both systems have a common origin and anatomically are closely related. This is the source of possible shared pathogeny of illnesses and parallelism of injury to both functions. This aspect has been successfully explored by clinicians who long ago paid attention to correlations between audiological damage and vestibular dysfunctions [5, 19-21, 63, 64, 67, 158, 161, 167, 168, 179). Just as important are the mechanisms by which the auditory and vestibular functions interact on the level of the central nervous system. Study of these mechanisms and quantification of their regularities shows promise for developing essentially new diagnostic tests based on discovering deviations which occur during pathological conditions. We can cite as an example research on the interaction of acoustic and otolithic systems [255] which showed that, if head position is fixed, the human eye is capable of following an acoustic phenomenon in darkness if the subject undergoes linear acceleration. Successful tracking requires accurate localization of the noise source in space and accurate evaluation of the relative speed with which it is moving. This is possible only by otolitho-acoustic interaction.

Nystagmus can change, for example, under the influence of additional acoustic and light stimulation. It is hypothesized that afferentation interaction occurs on the level of the truncus cerebri, particularly the diencephalon, while the modifying action of the noise is possibly accomplished at lower level -- in the medulla oblongata. This data was obtained in experiments on pigeons [159]. It is apparently possible that noise has a direct effect on vestibular apparatus receptors [120, 136, 137]. Nystagmometric research does not always account for the action of labyrinth factors, although there is a critical need to do this. Even the procedure by which the animal is immobilized can have an effect on nystagmometric characteristics /41 [208]. It is especially necessary to account for extralabyrinthine factors in studies which require nystagmus in "pure" form, since diagnosis depends on the accuracy of the characteristics obtained. But this is only one side of the problem. The other, more significant side is study of the effect of a particular labyrinthine factor on nystagmus in the norm and in pathological conditions and creation of new vestibulo-oculometric tests based on this study. An excellent example is the study of the effect of ocular afferentation on caloric nystagmus, which led to the creation of a test for fixation suppression of nystagmus, successfully used for differential diagnosis of the level of injury [390-392, 421].

Experimental stimulation of the vestibular apparatus is known to be associated not only with vestibulo-oculomotor reactions, but also with a whole set of other reactions: somatic, sensory, and vegetative [58, 59]. In virtually healthy humans, the latter can be expressed to varying degrees: under conditions of extreme exposure, some people experience motion sickness. Therefore applied nystagmometric studies in yet another

direction -- finding the correlation between nystagmometric data and vestibulovegetative instability -- seems natural [43].

Nystagmus and Otoliths

Voyachek's otolithic reaction, which has become a tradition in vestibulometric practice, is based on the interaction of otolithic organs and semicircular canals [35]. Interaction of otoliths and semicircular canals has not been extensively studied, although it has recently taken on great urgency [90, 91]. A priori, we can say that these organs must function in harmony, but it is very important to understand what disharmony can cause. Research on such questions is possible in experimental nystagmometry, but difficulties are involved. Primarily, there is no consistent opinion on whether nystagmus of otolithic origin is possible. Facts have been accumulated which indicate that nystagmus caused by stimulation of semicircular canals is affected by otolithic organs, but there is no consistent opinion on the mechanisms of these influences.

Eye movements consisting of alternating slow and fast phases were recorded under conditions when no shift in endolymph in the canals was expected, i.e. only otolithic receptors were stimulated [375, 276, 445]. We cannot say with certainty whether such reactions are caused directly by stimulating the otolithic apparatus. It is possible that otolithic afferentation only promotes the development of reactions whose genesis is related nevertheless to afferentation from canals. /42

One proposal suggests that linear acceleration in and of itself can cause cupula deviation [250, 251, 330]. However, there is serious opposition to this viewpoint [240]. We know that direct stimulation of the otolithic apparatus by linear accelerations (especially if a rabbit is swung in parallel pendular motion) does not cause nystagmus if the head is fixed in its usual position. Special conditions are needed to cause nystagmus during linear acceleration: in a rabbit, the head should be to the side; in a human -- the eyes should actively move to the side [382]. The very need to create special conditions casts doubt on the direct role of otoliths in nystagmus. Another hypothesis seems more acceptable: that the otolithic system has an overall regulating effect on ampullar reactions and on the system which causes them [35, 85, 102, 185, 186, 244, 461, 486-488]. Vestibular nucleus neurons directly connected to semicircular canal receptors react to rotation of the linear acceleration vector in the plane of the canals. This has been shown in experiments on decerebrated cats with angular acceleration completely eliminated [242]. Rotation of a human lying horizontal around a transverse body axis at a constant angular velocity (angular acceleration is eliminated) is associated with nystagmus [239, 241, 279, 280, 334]. At a velocity of 10 rpm, nystagmus has a constant direction, but its intensity is cyclic and changes over the total rotation time, depen-

ding on the periods during which the position of the binaural axis in the gravitation field is measured. At a velocity of 30 rpm, nystagmus becomes sign-variable and direction changes, also with a cyclicity corresponding to rotation time.

In cases when both semicircular canals and otolithic apparatus are simultaneously exposed to stimulation, rather complex reactions occur, analysis of which presents well-known problems. Changes in nystagmic reactions in such experiments are not always the result of the influence of otoliths. For example, it has been shown that centrifugal force produces changes in the threshold of cervical caloric nystagmus in pigeons [50-52, 76-79, 83, 339]. Cervical nystagmus in a pigeon can be considered an analog of ocular nystagmus. If a lateral canal is warmed locally (with the pigeon's head fixed, but with the canal in the horizontal plane and centrifugal force acting in the direction of the head-tail axis) an increase in the centripetal acceleration from 0 to 0.2 g raises the threshold of caloric nystagmus (cf. figure 16) in the direction typical for this stimulation [79]. If centrifugal force increases further, nystagmus ceases, but at 0.5 g nystagmus in the opposite direction develops. As centrifugal force increases, the threshold of reversed caloric nystagmus diminishes. The results of the experiments can be satisfactorily explained from the standpoint of the hydrodynamic theory of the cupula without discussing the role of otolithic organs: centrifugal force in these experiments seems to fulfill the same role as does gravity in an ordinary caloric test. At 0.5 g or more, conditions developed which can be compared with a change in orientation of a warmed canal -- its transition from horizontal position to a vertical plane. /43

How significant is the effect of otoliths during ordinary vestibular tests? It is probably minor or latent during an ordinary caloric test: hydrodynamic shifts in canals are of primary importance. Otherwise nystagmometric characteristics during caloric tests in supine and pronate positions would differ substantially, which is not the case [453]. During a standard clinical Barany test (the axis of rotation passes between labyrinths), the significance of centrifugal force cannot be disregarded [530].

The reduction in post-rotatory nystagmus duration with the head in an eccentric position during rotation has been described repeatedly [15, 196, 267]. However, otolithic effects can even intensify nystagmus. For example, in rabbits with so-called spontaneous nystagmus caused by severing the nerve of the lateral semicircular canal, the tilt of the head or DC electrical stimulation of the saccular and utricular macula are accompanied by a change in nystagmus intensity, and the effect

/43

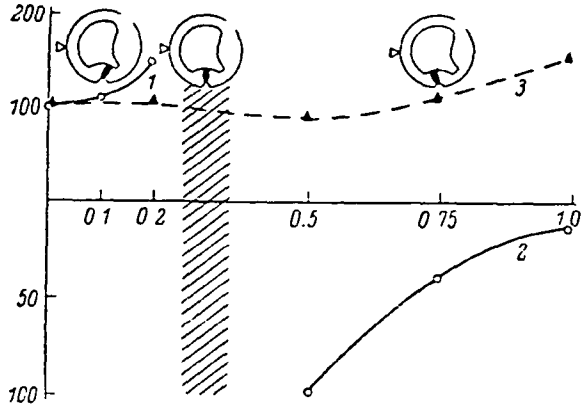


Figure 16. The effect of centrifugal force in the head-tail direction on the threshold of nystagmus in a pigeon's head (from [79].

1 and 2 -- Thresholds for nystagmi caused by thermal stimulation of the lateral semicircular canal; 3 -- Thresholds of galvanic nystagmus; X-axis -- centripetal acceleration, g; Y-axis -- thresholds, a percentage of the threshold in an immobile pigeon (curves 1 and 3) and of the threshold of the first reversed nystagmic reaction (for curve 2). Shaded area -- that in which there are no caloric reactions. Above -- diagram of a semicircular canal showing the point where the canal is warmed (triangle) and the direction of cupula deviation as a function of experiment conditions. The principal feature of the effect of centrifugal force on caloric and galvanic reactions is obvious.

/44

(intensification or diminution) is determined both by the direction of the tilt and the sign of the electrical stimuli [486, 488]. The complexity of the relationship between otoliths and canals becomes even more obvious in terms of the increased or unusual requirements imposed on the vestibular apparatus, as research on vestibular function under conditions of altered significance indicates [212, 213]. This research showed the need to account for the nature of the force (constant, variable), its absolute value, and the sign of the changes (increase, decrease), since all these factors taken as a whole define the effect of otolithic stimulation on nystagmus -- its inhibition or activation.

Quantitative research on nystagmus in a rabbit caused by angular acceleration during action of centrifugal force (eccentric rotation) revealed that changes in the dynamic characteristics of nystagmus under the influence of additional otolithic stimulation are rather stable [187]. After a single eccentric

rotation, standard rotation tests exhibited traces of otolithic effects for a long time. It is quite probable that stimulating otolithic organs promotes activation of adaptive processes [181-184, 437]. These facts may be interesting from the standpoint of applied nystagmometry: it is not impossible that eccentricity has a similar impact on human nystagmus.

Nonvestibular Forms of Nystagmus

The number of different nonvestibular forms of nystagmus described in literature is quite small, and listing them would take very little space. We will discuss a few of them, which, as one might assume, are of interest from the standpoint of future applied nystagmometric developments. The forms observed relatively recently include arthrokinetic nystagmus occuring during passive arm and leg movements [252, 253], as well as one variation of optokinetic nystagmus (OKN) -- "sigma-OKN" described in humans and certain animals as resulting from the illusion of movement of a visual image [219, 236, 333]. The connection between nonvestibular forms of nystagmus and the vestibular system is, in most cases, problematic. However, it is important to study them, since the principles of the mechanisms of reactions [480,481], may have something in common and because certain of these forms are already being used in applied research [235]. After cessation of vestibular nystagmus caused directly by a stimulus, inverse nystagmic phases opposite in direction are often observed [6, 88, 465, 473]. These reactions are assigned the prefix "post." Phase nystagmus occurring after post-rotatory nystagmus caused by negative acceleration is called "post-post-rotatory"; that after caloric -- "postcaloric" [176], etc. Sometimes there are /45
several phase reactions alternating in direction. Obviously, these reactions are not related directly to cupuloendolymphatic shifts. The hypothesis has been made that phased post-caloric nystagmus results from nerve processes in oculomotor centers formed long before the stimulation ceases [88]. It is possible that, regardless of the nature of the stimulation which causes the initial reaction, inverse nystagmic phases are not distinguished by their own particular mechanisms. Let us take an example which indirectly indicates the possibility that these processes exist in nerve centers which seem to compete with the mechanisms of the primary reaction. During prolonged exposure to angular acceleration, rotatory nystagmus may stop before conditions which promote the cupula's return to initial position are created, i.e. the reflex can be suppressed by some sort of competing process involving nystagmus and activated as the latter develops over time. These hypothetical mechanisms provide a basis for creating a model of nystagmic adaptation [437]. Data obtained during a study of vestibular nystagmus in a rabbit subjected to eccentric rotation supplements and confirms this model [183, 187]. We can hypothesize that the ability to adapt in and of itself may, in time, be a symptom suitable for diagnostic evaluation of the condition of the central nervous sys-

tem, just as is done now in audiology. It is quite probable that there is a commonality between inverse phase mechanisms and adaptation to prolonged acceleration. Study of similar phenomena observed during optokinetic stimulation -- counter-nystagmus [451] or, equally, of reverse post-optokinetic nystagmus (PON) subject to detailed research [16, 80, 81, 153, 154, 177, 477, 478] -- will aid analysis of inverse phases. Study of nonvestibular nystagmi can provide valuable information for discovering vestibular nystagmus mechanisms.

Naturally, one should always keep in mind that representatives of various types of animals in nystagmic reactions man exhibit features both similar and different. For example, adaptation mechanisms during prolonged angular acceleration are manifested to varying degress in cats and humans; in man, the extent to which the reaction diminishes is less pronounced. Secondary nystagmus, which is relatively weaker, is rarely evident [355].

Physiologists have paid a great deal of attention to so-called central nystagmus. This name covers apparently not one nystagmus, but a set of different reactions which have a common cause -- local electrical stimulation of a particular nystagmic zone. A nystagmic zone has been observed in the diencephalon, more dorsal and ventral than the anterior tubers of the lamina tecti [340, 413-415]. This zone affects vestibular nystagma. /46
Disconnecting it changes the threshold of post-rotatory nystagmus [467]. The diencephalon nystagmus zone inhibits ipsilateral and stimulates contralateral bulbar nystagmic centers [470, 471]. It has been established that nystagmus caused by stimulating the mesencephalic nystagmus zone in guinea pigs does not involve vestibular nuclei [326, 327]. Certain features common to central nystagmus caused by electrical stimulation of the diencephalon nystagmic center and vestibular nystagmus occurring during angular acceleration have been observed in experiments on rabbits [469]. Observation of various nystagmic zones and centers, stimulation of which causes central nystagmus and changes in nystagmic activity when some part of the central nervous system is disconnected, apparently should be considered as evidence that there is no special nystagmic center. It is precisely for this reason that identification of typical features of various central nystagmi shows promise from the standpoint of applied nystagmometry. The fact is that vestibulobiologists have long paid attention to so-called spontaneous nystagmi. Various tests have been proposed which help identify them, as have classifications based on qualitative description of these reactions. However, we must recognize that concepts of the origin and mechanisms of spontaneous reactions are clearly inadequate, and the diagnostic value of these symptoms is still negligible. The term "spontaneous" is often a signal that the origin of a given symptom is unknown. It is possible that careful study of central nystagmi will help increase the differential-diagnostic significance of spontaneous nystagmi.

So-called positional nystagmi are the most important spontaneous nystagmi in diagnosis. These mechanisms have been studied in depth and one might think that some of them can be shifted from the rank of spontaneous nystagmus to the category of reactions whose origins and mechanisms are known [44, 45, 233, 234].

Of course, OKN deserve the most attention of all vestibular nystagmi. Study of the relationship between vestibular and optokinetic nystagmic mechanisms is one of the important trends in the development of nystagmometry in the near future. Therefore, the next chapter of this book is devoted to certain aspects of this problem.

Nystagmography

Determining the role of particular formations in the development of nystagmus, deciphering the mechanisms of vestibulo-oculomotor reactions and the relationship between various types of nystagmus, and many other tasks, including diagnostic nystagmometry, are impossible without precise recording of nystagmus. Numerous methods have been proposed which are distinguished

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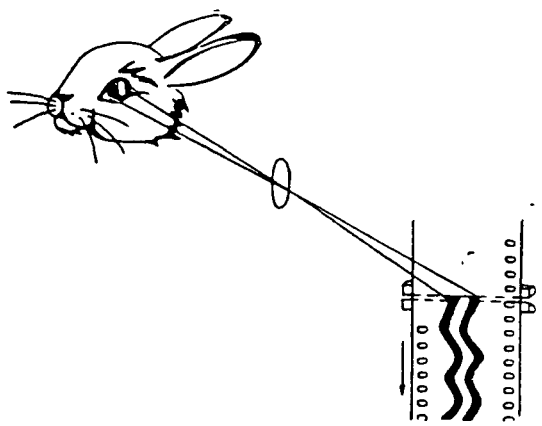

Figure 17. The principle of photonystagmography.

The image of the eye is processed on photographic film through a slit. Inversion is ensured by moving the film at a constant rate, time interval by momentary closure of the objective (or by additional illumination) over different times. The horizontal component of eye movement is recorded continuously. A vertical mark fixed on the eyeball helps eliminate distortions if the eye should turn around the naso-occipital axis, and also increases recording contrast. This method produced the recordings in figures 2, 13, and 42 A,

according to how eye movement is transformed into a motion curve, according to measurement limits, or according to sensitivity. Nystagmometry began to be used at the end of the last century; since then, development of new procedures, whose description and comparative evaluation appear in several anthologies and in special studies devoted to ocular motility [19, 31, 100, 101, 103, 146, 174, 205, 213, 320, 500, 517, 534], has not ceased.

Mechanical, optical, inductive, and bioelectrical techniques are differentiated in terms of the way in which ocular movement is transformed into a graph. Mechanical techniques include those in which the eye is directly connected to a recorder using levers, needles, hydraulic, pneumatic, or other types of transmission [1, 48, 62, 97, 481, 585].

Several electromagnetic techniques for recording nystagmus have been proposed [106, 293, 384, 519, 543]. In the simplest version, a ferromagnet is attached to the eyeball and a magnetic recorder is placed close to the eye [543]. Subsequent development of this trend has led to use of high-frequency electromagnetic signals modulated by ocular movement.

The connection between the eye and the recorder is accomplished by optical means using a light packet reflected from the surface of the eye or from a mirror attached on the eyeball. Direct photography with temporary inversion, as well as cinematography in visible, infrared, or ultraviolet light, is used. These procedures also include photoscanning pupillography [204], high-speed cinematography [258], slit photonystagmography (cf. figure 17) [140]. If a mirror hasbeen attached to the surface of a closed eyelid [32, 33], the change in curvature of the eyelid during movement of the cornea beneath it is measured, not the turn of the eyeball. Mirrors and microlamps attached to the eyeball with contact lenses or suction cups are used [256, 257, 259, 291, 306]. Photoelectronystagmography is a modification of photographic methods [260, 279, 496, 514-516].

Bioelectrical techniques include electromyography and /48
electronystagmography. The latter is a special application of electro-oculography and ensures a recording accuracy of at least ±1.35° when the eye turns in a ±25° range [535]. Electronystagmography is becoming increasingly common in nystagmometric research. Therefore, a vast amount of literature has been devoted to related problems -- calibration, electrode arrangement, amplifiers, recording systems, as well as to quantitative processing of electronystagmograms (ENG's).

Electro-oculography is based on the properties of the eyeball, which is an electrical dipole: its anterior pole is charged positively; its posterior, negatively. The difference in potentials reaches 10-30mV [440]. This difference, called the corneo-retinal potential, is variable and depends on

various factors [216, 408, 409]. The difference in potentials creates an electrical field around the eye. Changes in the configuration and position of this field can be observed using electrodes attached close to the eyeball. The ENG essentially reflects the nature of the change in electrical field due to ocular movement. If the electrodes are arranged symmetrically relative to the optical axis of the eye, the change in electro-oculographic potential is proportional to the sine of the angle of eye rotation (provided that electrodes are at an equal distance from the anterior pole of the eye and that version takes place in the plane of the electrodes and the optical axis of the eye) [174]. A preamplified signal from the electrode is sent to a recorder or an oscillograph screen [225, 317, 380]. When the horizontal component is recorded, the electrodes are arranged at the outer and inner corners of the eye (monocular separation) or at the outer corners of both eyes (binocular separation). In an acute experiment with animals electrodes may be attached to soft tissue (e.g. to eyelids, as is done in experiments on guinea pigs [249]), but in a chronic experiment electrodes inserted into the ostial borders of the eye socket are used [81]. Cutaneous electrodes are also quite acceptable. There is no uniform opinion regarding amplifier pass bands. Sometimes attempts are made to use the largest possible time constant (e.g. 2 sec [227]). In other cases a low value (e.g. 0.8 sec [174]) is satisfactory. Arrangements specially intended for signal differentiation [349, 350, 402] are also used. Maximum accuracy in recording slow components of nystagmus requires selection of an amplifier which ensures that low-frequency signals travel with minimum distortion. The corneo-retinal difference in eye-dipole potentials is not constant. It varies rather slowly under the influence of various factors, of which illumination is the most important. /49

Electronystagmography makes it possible to record horizontal and vertical components of ocular movement.

Major obstacles to electronystagmographic research on animals arise if it is necessary to evaluate amplitude characteristics. These obstacles result from calibration problems because of which we usually resort to evaluating amplitude characteristics in units of electrical potential or limit ourselves to measuring frequency, which reduces the value of the research. For example, frequency cannot be used if the activity of the peripheral network in the vestibular system must be compared in terms of nystagmus and the reactions differ in amplitude [555, 556].

The problem of calibrating ENG's deserves detailed consideration. Calibration methods described in literature can be divided into direct and indirect. To calibrate human ENG's, we usually use electro-oculographic potential recorded when the eye moves during a shift in points of fixation, the angular distance between which is known [174, 215, 226, 285, 535].

Methods in which a calibration signal is obtained as a result of eye version at a specific angle can be called direct. Indirect methods include those in which electronystagmograms with approximated characteristics serve as the calibration standard. For example OKN [281], as well as nystagmus recorded during accelerated rotation in light with eyes open [352] (vestibulo-optokinetic nystagmus) is used as a reference nystagmus. In individual instances, indirect calibration is used in research on humans [103, 351]. Research on animals generally uses indirect calibration, because in animals it is almost impossible to produce active movements with assigned characteristics. The procedure used in one article to study saccadus in cats [245] can be considered an exception. This procedure somewhat resembles calibration used in humans, but obtaining a calibration signal involves significant difficulties: the experimenter visually determines that the animal's eye is turning in the required direction and at the required angle.

Indirect calibration using OKN is based on two speculative prerequisites: 1) OKN SSC is stable during the reaction, 2) OKN SSC equals the speed at which the optokinetic stimulus (OKS) is moving. The first prerequisite must be checked, since optokinetic reactions may be suppressed in humans [451]. The second prerequisite is also questionable. There exists data which indicate that OKN SSC is slower than stimulus speed [75, 270].

A B C /50

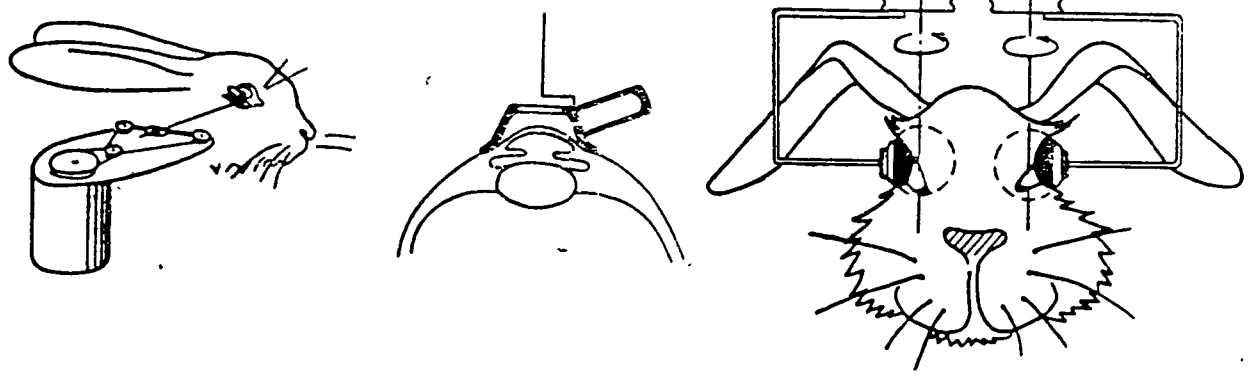

Figure 18. Device to produce calibration signals.

A -- General view of the simplest version of a monocular calibration device (from [22]); B -- Suction cup with a stem on the eyeball; C-E -- binocular calibration device (from [24]). C shows the relationship of the animal's head and the calibrator while the calibration signal is being produced to evaluate horizontal nystagmic reactions.

In other words, the competence of indirect calibration must be tested. It can be checked, for example by combining electronystagmography and photonystagmography [108, 140]. It is much more preferred to replace indirect calibration methods with a technique based on recording electroo-oculographic potential during passive (forced) version of the eyeball [22-24, 131, 132]. Forced version of the eyeball has been used in experiments on animals in the past to study the resistance of

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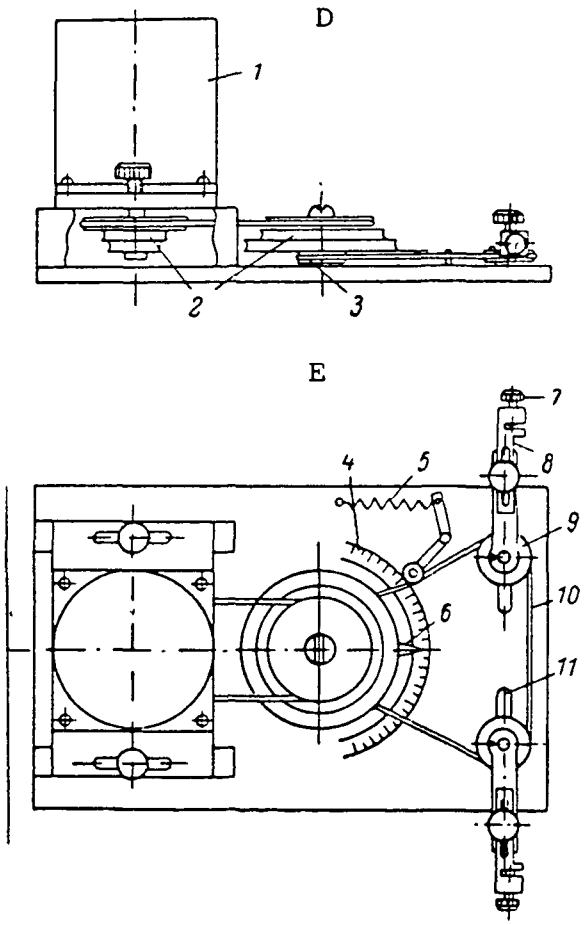

Figure 18 (cont.)

D and E show a diagram of the device; 1 -- Reversing motor; 2, 3, 9, 10 -- Reducing gear and transmission details; 4 -- Transporter with rotation amplitude indicator (6); 5 -- Round drive belt tightening mechanism; 7 and 8 -- Details of the lever which transmits force to the suction cup; 11 - Slot for adjusting the distance between version axes according to the distance between eyes.

extraocular musculature [548], changes in electro-oculographic potential during a shift from darkness to light, and rhythmic eye illumination [403]. This research is usually accompanied by eye injury. For example, during a study of darkness adaptation [383], a rabbit's eye was turned by tightening a thread sewn to the cornea. Naturally, such methods should not be used to calibrate ENG's.

The calibration method described below [24] is executed with a special device and is has several beneficial features. The procedure is not traumatic. It provides a calibration signal regardless of illumination conditions, i.e. during adaptation both to light and to darkness. Eye versions may be oriented strictly in the plane in which the ENG is being recorded. The size of the angle at which the eye turns, as well as movement speed are set by the experimenter. A signal can be produced which is suitable both for evaluating electronystagmographic material and for ENG's recorded binocularly. Continuous movement differing in form, frequency, and amplitude can be recorded and a calibration electro-oculogram (EOG) with parameters close to an actual ENG can be produced. The basic structural feature of the calibrator (cf. figure 18) is the relative location of the drive mechanism and the eye. This allows turning axes to coincide, so that eye movement corresponds to the preassigned movement. The axis of the driven shaft (cf. figure 18, 9) coincides with the axis in which the eye turns horizontally. Force on the drive shaft is transmitted from the motor's rotor by a reducing gear and a transmission system. The driven (9) and driving (3) gears are equal in diameter. Because the driven shaft and the eye are coaxial, three links, i.e. the driving shaft, the driven shaft, and the eye, turn synchronously and, as a result, passive (forced) eye movement is equivalent to assigned movement. A scale on the transporter (4) monitors the turning angle. This is how a monocular calibration signal was obtained for an ENG of a rabbit. If there is a need for binocular calibration, both drive shafts, which are connected by a common round drive belt (10), are used. Distances between the axes of the driven shafts are adjusted to the individual distance between the turning axes of the animal's eyes by shifting the driven axes in the slot (11). Another relative arrangement of levers is possible. The angle between their horizontal planes can be reduced, which is necessary to calibrate EOG's of animals with different relative arrangements of the optic axis (cat, dog). The calibrator uses a staged reversing motor which achieves a constant drive shaft speed over any time interval and can almost instantaneously change rotation direction. The motor is controlled by sending impulses from the electronic controller, whose detailed description has been published [24].

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Experimental testing of this calibration method involved determining the reliability of the procedure and identifying possible sources of error and artifacts, as well as conditions

which would help prevent them.

The primary results of the procedural test are summarized below.

1. With the suction cup centered, repeated passive abductions and adductions of the eye at the same angle change the recorded potentials equally (cf. figure 19). It follows that obtaining a calibration signal (CS) does not require a large number of passive movements. 2. The calibration factor can be calculated using the arithmetic mean of signals obtained

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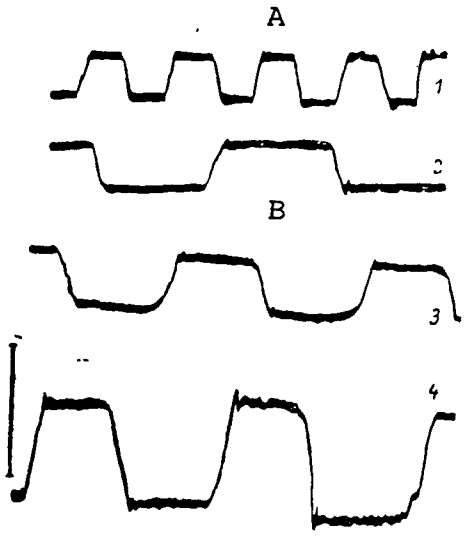

Figure 19. Electro-oculographic potentials during direct calibration -- passive version of the eye of a rabbit -- in two experiments (A and B) (from [132].

In experiment A, two recordings were made at the same passsive version angle. The stability of the calibration signal during repeated abduction and adduction of the eye (1) and the reproducibility of results after repeated placement of a suction cup on the animal's eye (2) are shown. In experiment B, calibration at different turning angles: (3) 15° and (4) 30°. Calibration -- 1000 mkV.

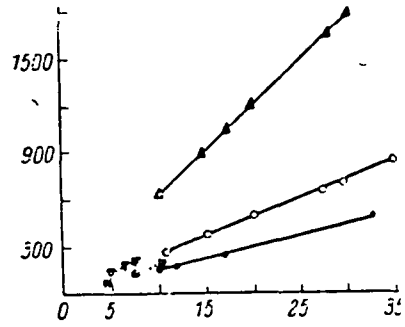

Figure 20. CS amplitude as a function of passive (forced) eyeball turning angle (from [132]).

Results of experiments on 5 rabbits (identified by different symbols). X-axis -- Eye turn CS amplitude, °; Y-axis -- CS amplitude, mkV.

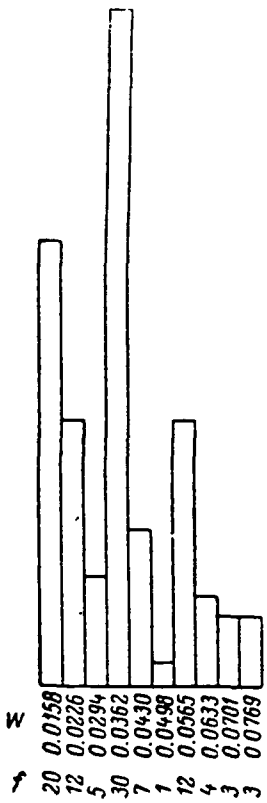

Figure 21. Histogram of calibration factors R from 20 experiments on 13 rabbits[132].

W -- lower class boundaries, f -- the number of cases. $\bar{x} + \sigma = 0.397 \pm 0.176^{\circ} \cdot mkV^{-1}$. Asymmetry and excess uncertain.

during eye abduction and adduction. 3. Care must be taken that the suction cup comes in contact with the eye along the limbus. 4. Mean arithmetic amplitudes of calibration signals (mkV) during repeated calibration with angle of passive eye version constant are indistinguishable within the limits of a single experiment. 5. The calibration factor ($^{\circ} \cdot mkV^{-1}$) is highly reproducible if electrode position is unchanged. (The differences in repeated experiments on the same animal are commensurate with the accuracy of visual evaluations of an ENG taken with a 16X oscillogram enlargement recorded on a circuit-oscillogram). 6. CS amplitude increases linearly as passive version of the eyeball increases (at angles of ±15°). 7. The slope of the increase in CS as version angle increases is individual, i.e. the calibration factor is individual. Therefore, errors /54

in evaluation of ENG amplitude characteristics are possible if they are being evaluated for subsequent comparison with reactions of different specimens.

Figure 20 illustrates the last two points. Each point on the curve is the average CS for several recordings (given a fixed version angle). Amplitude increases linearly as the angle increases, which demonstrates that the calibration factor can be reliably reproduced for a given animal within the limits of one experiment. The calibration factor (in $^{\circ}\cdot mKV^{-1}$) can be calculated as the cotangent of the curve's slope. Because of this linear relationship, once we have calculated the slope of the curve at two points, we can find the CS for other angles.

It is possible that the linear relationship between amplitude and the version angle of the eyeball is retained even at large angles, as in man [174, 216, 535]. However it is hardly worthwhile calibrating at angles above $\pm 15^{\circ}$.

Additional check tests have also been set up [131]. Calibration factor as a function of outlet electrode position was checked. Experiments were conducted under varying conditions: in some experiments, electrodes were removed and then replaced in an attempt to restore them to their original position; in others, electrodes were deliberately moved relative to their initial position.

In particular, the assumption, well-known from literature [216], that tapped potential is a function of electrode position has been confirmed. Since the retractor muscle ennervated by the oculomotor nerve is rather active in rabbits [581], calibration factor as a function of the level of activity of this muscle, which shifts the eyeball in its socket and, consequently, changes the geometry of the relationship between the calibrator and eye, was checked. It has also been shown that the average calibration factor in a rabbit is $0.04^{\circ}\cdot mkV^{-1}$. This value may be useful only for approximating ENG when individual calibration is, for some reason, impossible. However, the substantial spread (cf. figure 21) of individual results ($0.0158\text{-}0.077^{\circ}\cdot mkV^{-1}$) represents a serious obstacle to the use of a mean arithmetic calibration factor in research which requires accurate ocular movement parameters. /55

Development of a direct ENG calibraton procedure for animals has made it possible to check the competence of the indirect calibration method and the validity of assumptions underlying use of ONK as a reference nystagmus. A significant difference in individual mean OKN SSC's has been observed, as has the instability of the SSC within an individual ENG (variation factor 26-27%). The mean OKN SSC in most cases lags behind stimulus speed (the latter equaling $30^{\circ}\cdot sec^{-1}$). Indirect calibrations are rather important, since calibration error can cause erroneous conclusions.

We can cite a study [281] in which OKN was to calibrate ENG's used in experiments on animals. This work involved experiments on cats in which the calibration reference was an OKN produced at a rate of optical stimulation equal to $36^{\circ}\cdot\cdot\sec^{-1}$. It was noted that this speed was selected because the OKN was sufficiently stable at it, while at $18^{\circ}\cdot\sec^{-1}$ it was irregular, and when speed increased to $60^{\circ}\cdot\sec^{-1}$ OKN SSC diminished. (The fact that OKN SSC in a rabbit lags behind optokinetic stimulus speed has been noted in several works. Reference [270] establishes that it lags farther the greater the stimulus speed.) Reference [131] has shown that OKN SSC in a rabbit does not stabilize, even during prolonged (30 sec) stimulation and that the difference between SSC and stimulation speed can be quite substantial. Since OKN in humans is also not always stable [451], we should regard with caution recommendations to use indirect calibration in studies on humans.

The possibility of using still another reaction -- VOKN -- as a reference signal has been tested. To produce this reaction, rabbits are subjected to positive angular acceleration with eyes open in light [131]. Experiments showed that, in most cases, the maximum SSC of vestibulo-optokinetic nystagmus was actually equal or close to rotation speed. However, it may also lag -- by considerable amounts at times.

A study has been done on the possibility of using a monocular calibration factor ($^{\circ}\cdot mkV^{-1}$ to evaluate an ENG recorded binocularly [131]. The premise is as follows. OKN SSC, expressed in angular units ($^{\circ}\cdot\sec^{-1}$), does not depend on the potential tapping method and, consequently, is identical in two OKN's, one of which was recorded monocularly, the other binocularly. This means that OKN SSC can serve as a bridge encouraging use of a monocular calibration signal to evaluate a binocularly recorded ENG. Each experiment recorded the following: an ENG for vestibulo-optokinetic alignment nystagmus (VOKNC)[1] (binocularly), CS (monocularly), OKN ENG (binocularly), and OKN ENG (monocularly). VOKNC SSC produced the maximum values, OKN SSC the average (in $mkV\cdot\sec^{-1}$). /56

Since the results were qualitatively identical, we can limit our discussion to examples given in table 2, which demonstrate the transition from monocular calibration to evaluating binocularly recorded ENG's. The validity of this transition was confirmed by check tests in which VOKNC's were

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1 VOKNC is a reaction to the combined (vestibular and optokinetic) stimulation provided that the stimuli coincide in sign (e.g. during accelerated rotation in light with open eyes). Chapter 2 discusses these reactions.

TABLE 2
TWO EXAMPLES OF EVALUATING BINOCULARLY RECORDED VOKNC IN A RABBIT USING CS'S OBTAINED MONOCULARLY (132)

Rabbit (exp.) No.	Record No. and Type of reaction	Potential tapping condition	Obtained directly from experiment data,	Figure obtained by calculation, $^{\circ}\cdot sec^{-1}$
1	1. VOKNC	Binocular	A (max. SSC) = 922 $mkV\cdot sec^{-1}$	$A_1 = 30.4$
	2. OKN	"	B (ave. SSC) = 596 $mkV\cdot sec^{-1}$	$B_1 = 20.0$
	3. OKN	Monocular	C (ave. SSC) = 756 $mkV\cdot sec^{-1}$	$C_1 = 20.0$
	4. KS	"	R = 0.0264$^{\circ}\cdot mkV^{-1}$	
2	1. VOKNC	Binocular	A (max. SSC) = 1359 $mkV\cdot sec^{-1}$	$A_1 = 30.1$
	2. OKN	"	B (av. SSC) = 1206 $mkV\cdot sec^{-1}$	$B_1 = 26.9$
	3. OKN	Monocular	C (ave. SSC) = 1033 $mkV\cdot sec^{-1}$	$C_1 = 26.9$
	4. KS	"	R = 0.0259$^{\circ}\cdot mkV^{-1}$	
	5. VOKNC (control)	"	M (max. SSC) = 1225 $mkV\cdot sec^{-1}$	$M_1 = 31.8$

NOTES: 1. The order of calculation (e.g. for the first experiment): $C_1 = C\cdot R = 20^{\circ}\cdot sec^{-1}$; $B_1 = C_1$ (speed in angular units does not depend on potential tapping method); from ratio $B/B_1 = A/A_1$ we can find $A_1 = AB_1/B = 30.4^{\circ}\cdot sec^{-1}$.

2. In the second experiment, a reference recording, 5, was made. Calibration factor R can be used to evaluate its CS: $M_1 = M\cdot R = 31.8^{\circ}\cdot sec^{-1}$. Comparing A_1 and M_1 shows a satisfactory correlation of results with this ENG evaluation method.

recorded both binocularly and monocularly. The coincidence between the SSC's for the two VOKNC (one calibrated directly, the other indirectly) was quite satisfactory. Thus direct monocular calibration can be used to evaluate binocularly recorded reactions by applying indirect technique. However, the indirect method used in this case cannot be combined with indirect methods discussed above, which are based on a priori and, as we have seen, erroneous assumptions that OKN SSC and stimulus speed are equal.

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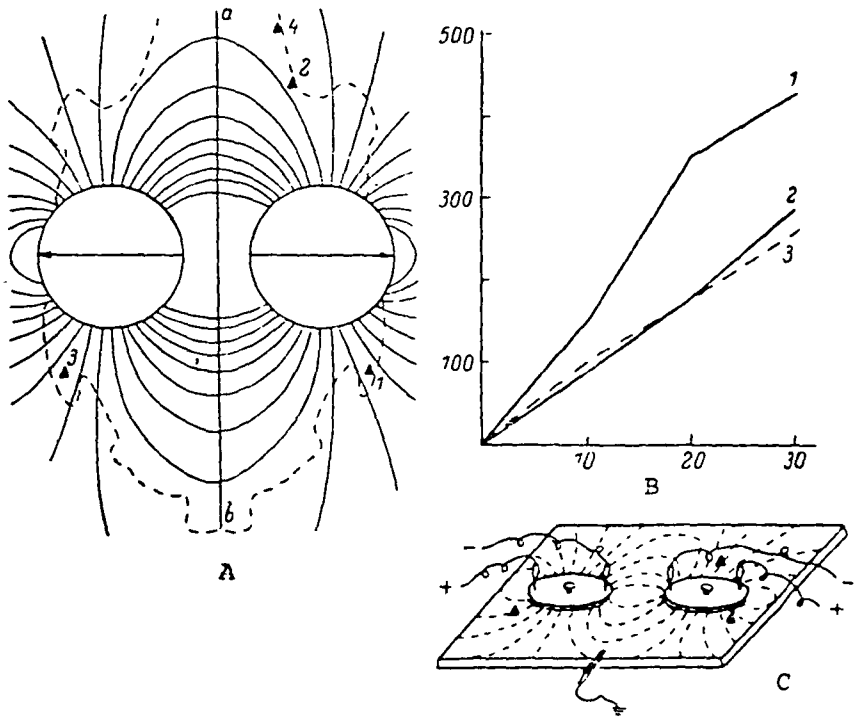

Figure 22. Modeling electrical fields on electrically conductive paper (from [131]).

Equipotential lines of a "rabbit" (A), difference in potential as a function of eye version angle (B) and model structure (C). In A the broken line shows the contour of the skull; solid lines are equipotential lines; arrows indicate the dipole electrical fields; ab -- the naso-occipital axis; triangles represent the position of outlet electrodes in monocular (1 and 2 or 1 and 4) and binocular (1 and 3) electronystamography. In B: X-axis -- the angle of concomitant turn of the model's electrical dipoles, °; Y-axis -- difference in potentials on electrodes, mV (absolute value of the potential has no meaning). The charts were produced at different tappings: 1 -- from points 1 and 3; 2 -- from points 1 and 2; 3 -- from points 1 and 4.

Physical modeling of eye-dipole electrical fields [131] using electrically conductive paper is widely used to model electrical processes [193]. This makes it possible to produce maps of equipotential lines (cf. figure 22) for electrical fields for lateral (rabbit) and frontal (man) eye position. In particular the model confirmed that the calibration factor obtained monocularly for a rabbit cannot be used directly to evaluate binocularly recorded ENG's. Even more significant is the difference between monocular and binocular tapped potentials in man. It is nearly double. Data obtained

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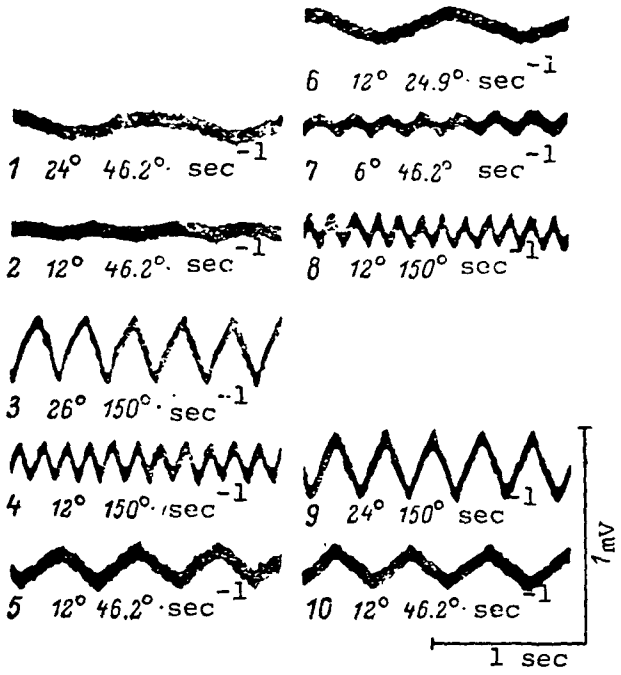

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Figure 23. Comparison of CS in two calibration methods -- monocular (left) and binocular (right) -- as well as in two methods of signal tapping -- binocular (top) and monocular (bottom) (from [241].

Calibrator working conditions (turning angle, speed) in which each record was produced are given (1-10). Right bottom -- time and potential scales.

from the model correlates satisfactorily with the results of experiments on rabbits [24] in which both calibration methods -- monocular and binocular were used. Figure 23 shows an example of recordings made on a single animal. In this case, high version speeds are commensurate with nystagmus FC speeds; low speeds with SC speeds. It is clear that potentials are sufficiently stable within the limits of each recording. At identical amplitudes of passive eye version, CS does not depend on eye movement speed. In passive version of one eye, there is no direct, proportional relationship between version angle and CS value if potentials are recorded by binocular tapping.

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If recording is monocular, the relationship between CS and turning angle is strictly proportional. Passive movement of two eyes is associated with an increase in CS proportional to turning angle during both monocular and binocular recording methods. If potential is recorded monocularly, CS does not depend on whether one eye or two underwent passive version. For binocular recording, in contrast to monocular, this does matter: signal amplitudes at identical angles depend considerably on whether one or both eyes have been subjected to turning.

Of course, there is no all-purpose procedure for recording nystagmus which is equally suitable for solving all the problems associated with studying vestibulo-oculomotor reactions. Some techniques make it possible to produce a recording in the form of a chart with path-time coordinates which must be processed further. Others provide a particular finished result in the form of a motion characteristic (nystagmus frequency [560]), slow and fast component speed [349], et al.). The choice of procedure should be determined by specific research conditions and assignments. Procedures differ in terms of interference-resistance and sensitivity.

Sensitivity is the key indicator of a procedure. Most vestibulometric techniques are based on the use of super-threshold stimuli and, consequently, on recording rather pronounced reactions. Threshold stimuli are used rather infrequently [157]. It is possible that wider use of sensitive techniques for recording eye movements will promote growth of the sphere of application of threshold tests under clinical conditions.

When versions within the limits of 1° (or more) are being recorded, electronystagmography and photoelectronystagmography give good results. At amplitudes from 0.05 to 0.01°, photoelectronystagmography is acceptable, but at small amplitudes (from 0.01°) special techniques using contact lenses, electromagnetic devices, etc. are needed.

Virtually any procedure can be used to record horizontal nystagmus. Electronystagmography is more convenient for recording vertical nystagmus.

Until recently, rotatory nystagmus and other torsional movements were recorded only by various types of photo- and cinematic recording and evaluating these reactions was quite difficult. Details on the techniques and devices for visual observation of otolithic reflexes in the frontal plane are covered in reference [89]. Lack of a simple and reliable recording technique is the reason why only a few published research articles [37, 38] have been devoted to the rotatory form of eye movements, while applied literature has not yet dealt with quantitative evaluation of rotatory nystagmus.

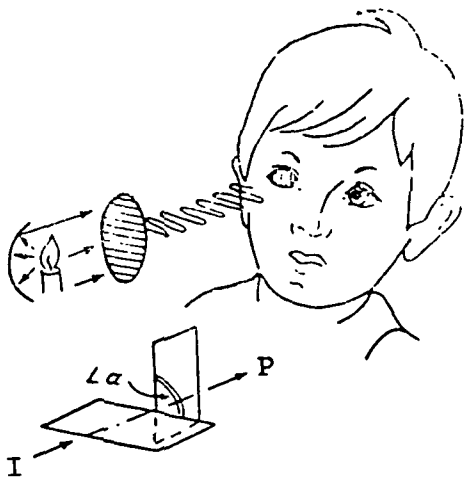

Figure 24. The principle of recording rotatory nystagmus (from [57 and 125]). /60

Only part (II) of a general light stream (I) falls on a photoreceiver mounted on the eyeball. This partial light stream is proportional to the cosine of the angle (α) between the polarization planes of the two polarizers. One of the polarizers is connected to the light source, which is fixed in head coordinates; the second turns together with the eye. $P = I \cdot \cos \alpha$.

A *new method has been proposed for recording rotatory re-* flexes [57, 125], which, as one might expect, helps fill the gap in the study of rotatory nystagmus and serves as the basis for applied research dealing particularly with the relationship of semicircular canals. The method is based on using polarized light. If a stream of light arriving at the receiver passes consecutively through two polarizing filters, the amount of light (receiver illumination) will depend on the mutual orientation of the polarizing planes (cf. figure 24). If the polarizing planes turn relative to one another, illumination changes proportionally to the cosine of the turning angle, i.e. if planes are parallel (angle 0°), illumination is maximum, but if one plane turns 90° relative to the other, it is minimum.

The receiver is a miniature photoresistor covered with a polarizing layer. It is mounted on an anesthetized eyeball using a suction cup attached beforehand to the eyelid so that it would not be shifted by blinking. A small amplifier, as well as the light source with polarizer, are mounted on a mask placed on the subject's head. A signal from the amplifier reaches the self-recorder. Figure 6 depicts an example of rotatory nystagmus recorded in a human by this method.

The device is adjusted before the study by turning the polarized light source already attached to the subject's head. The source's position relative to the head remains unchanged during recording. Therefore only signals resulting from movement in the head coordinates of the polarized receiver mounted on the eyeball are recorded.

If we use the cosinusoidal law of illumination as a basis, the best recording conditions are created by shifting the polarizing planes 70° relative to one another beforehand. Two goals are thus achieved: the relationship between signal and *eyeball version angle (in a given version range, i.e. ±15°)* becomes virtually linear, and the signal's sign depends on /61

movement direction (clockwise or counterclockwise).

In practice it works as follows. Once the suction cup with the receiver is mounted on the eye and the mask with the light source and amplifier is attached to the subject's head, we connect the receiver to the amplifier's inlet with fine wires which do not obstruct eye movement. Then the amplifier is connected to the self-recorder. Source polarizing planes are then turned until the signal from the receiver reaches minimum (which corresponds to polarizing planes turning 90° relative to one another). Then the angle is decreased to 70°. The recording is made in this position. Calibration signals obtained when the source turns ±10° are recorded twice (before and immediately after the study). Such calibration is necessary because, all other conditions being equal, illumination depends on the distance between the light source and the eyeball, while the latter's position in its socket can vary individually. In this form the procedure can provide recordings of human eye versions in the frontal plane only if the eye executes no other movements at the same time. Since movements are almost always complex, version in the frontal plane turns out to be latent.

Two signals caused by different movements (e.g. horizontal turning and rotatory turning) and different physical phenomena (e.g. a decrease in the angle at which the stream of light hits the receiver and an increase in the angle between the polarizing planes) will be virtually indistinguishable.

To eliminate the effect of similar interference on a useful signal, an additional receiver, which, unlike the primary receiver, does not have a polarized coating, is placed on the suction cup. The additional receiver, close to the primary receiver, reacts to all eye movements except version in the frontal plane, since polarizations are irrelevant for it. The signal from the additional receiver arrives at the light source's brightness controller according to the principle of negative feedback. In all cases, if any sort of movement other than rotatory even barely starts, then, in accordance with the signal from the additional receiver caused by the change in the latter's illumination, then source brightness changes. Interference is quickly compensated and is not reflected on the rotatory component recording, since the amount of light hitting the main receiver depends only on the amplitude of the rotatory eye movement. A diagram of the device is shown in figure 25. From the standpoint of applied nystagmometry, the following features of this method are important: 1) the procedure provides a visual signal in real time; 2) it is interference-resistant and ensures that the rotatory component will be rendered in "pure" form, regardless of the complexity of the actual movement; 3) it ensures high enough sensitivity (angles from 1° are recorded) and a virtual linear relationship between the recorded signal and a turn of the eye within ±15°. /61

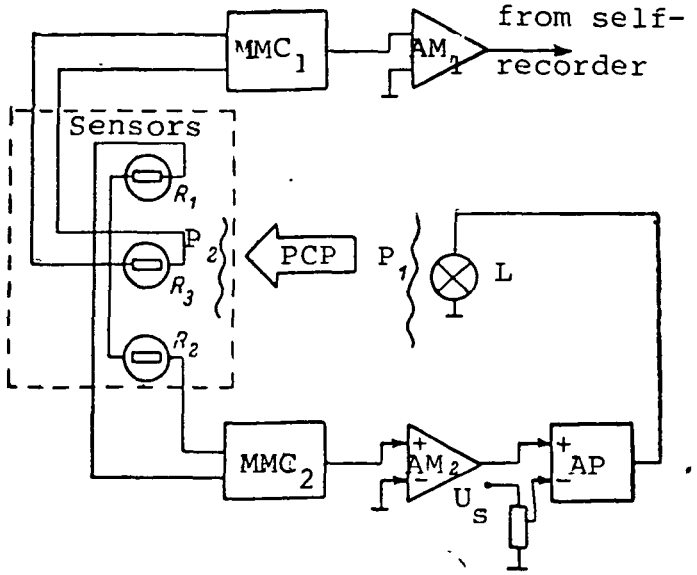

Figure 25. Block diagram of a device to record rotatory nystagmus (from [125]).

Photo-resistor R_3 with polarizing filter P_2 reacts to eye rotation. Photoresistors R_1 and R_2, which sense negative feedback signals to the polarized light source L and polarizing filter P_1, react to all other movements. All sensors (boxed by a broken line) are mounted on the eyeball. The remaining components are fixed in the coordinate systems related to the subject's head. PCP -- polarized stream of light; MMC_1 and MMC_2 -- bridge measuring circuits; AM_1 and AM_2 -- DC amplifiers; AP -- DC power booster; U_s -- reference voltage.

We must mention one more significant feature of the method: the principle it uses can be successfully applied to recording movements in any plane, i.e. not only rotatory, but horizontal and vertical as well. Simultaneous recording of three components can be ensured by a design combining three identical devices: three sets of receivers on one suction cup, oriented in the horizontal (to record the horizontal component), sagittal (to record the vertical component), and frontal planes. Each set should have a separate polarizing illuminator. Simultaneous recording makes it possible to obtain a complete idea of all the details of complex eye movement.

The method developed is an important step on the path of creating vestibulomotor tests required for quantitative evaluation of the function of vertical semicircular canals and of the otolithic system. The new method may be of great value in studying various forms of spontaneous nystagmus, many of which have a rotatory component. In particular, rotatory paroxysmal /63

positional nystagmus occurs during cupulolithiasis of the posterior vertical canal [176, 533]. It is possible that quantification of this nystagmus will make it possible to obtain new information on the pathogenesis of this illness, rarely discernible and still quite puzzling.

The Significance of Quantitative Study of Nystagmus

Quantitative evaluation of various forms of nystagmus is necessary for physiological research on the vestibular function, to identify pathology, et al., but it is worthwhile only if a good recording is made and if several conditions are met. The most important of these conditions are: consideration of the intensity and sign of the vestibular stimulus; an idea which receptors are primary in the reaction; careful selection of reaction parameters to be evaluated; measuring these parameters with accuracy adequate for the assigned research; and, finally, eliminating additional factors which can affect the result. For example, to eliminate the effect of predominant positive acceleration on post-rotatory nystagmus, we must ensure a speed with low acceleration and prolong the interval between positive and negative accelerations [227]. Careful observation of pauses between caloric tests is required [505].

A nystagmogram is a source of information on the direction of the reaction, the rhythm, frequency, amplitude and speed of slow and fast components and other characteristics of the nystagmic reflex. Most important from the standpoint of applied nystagmometry are those characteristics which can be used to evaluate the condition of the vestibular system. It is quite understandable that concepts of a norm are needed. The job of statistically describing a norm is not simple. First, the very concept "norm" relates to a specific population and is connected with the age of the subjects [412]. Second, it is suitable only for a certain research technique, while lack of standards in procedures drastically complicates the task, as many researchers have repeatedly indicated [19, 68, 174, 453]. Among the tests which should be standardized first is BT, the most commonly used in worldwide clinical practice [230, 268, 380]. Just as important is standardization of techniques used to quantify results, especially in daily diagnostic practice. Traditional tests should preferably be as informative as possible. One important step in this respect is a diagnostic model which makes it possible to obtain additional information on the condition of the vestibular system during a traditional BT [124]. Chapter 4 of this book deals with this model.

Quantitative evaluation of nystagmus is necessary not just for diagnostic research. It is absolutely essential to improve the tests themselves and to develop new ones. Let us look at certain examples. In a rotation test, done in its traditional form with a trapezoidal program, cupuloendolymphatic displacement occurs in the acceleration area and, after constant rota-

tion speed is reached, the cupula slowly returns to its original position. This last phase can be called passive, since acceleration is no longer a factor. In the dynamics of nystagmus characteristics, we can also identify two areas, one of which is related to the active displacement phase, the second -- to the cupula return phase. The first area contains more information about the hydrodynamics of the semicircular canals and about the condition of the ampullar receptor apparatus than does the second, since the central influences (particularly adaptation) on nystagmus characteristics have not yet been successfully represented. Special research has shown that the second-phase time constant does not change significantly during peripheral vestibular dysfunction [29, 42]. It is understandable that a vestibulometric test in which both phases of cupula movement are active, i.e. sign-variable stimulation is required, may turn out to be preferable. One alternative (sinusoidal rotation) was used with particular success during creation and testing of a model of oculovestibular interaction [419]. Sign-variable stimulation in which each labyrinth is stimulated separately -- the so-called sinusoidal caloric test [507, 508] shows particular promise for applied research. In this test, the irrigating liquids' temperatures equal those in standard bithermal testing (i.e. they differ from body temperature by ±7°C) and, strictly speaking, the stimulus itself is gradual, but not sinusoidal. However, test developers have selected an irrigation time such that the dynamics of cupuloendolyphatic shift are close to sinusoidal. This has been accomplished by relying only on the dynamic nystagmometric SSC characteristic-envelope. Subsequently another sinousoidal test was successfully developed in which the liquid is replaced by air [509, 510]. In general air-based caloric stimulation techniques were proposed as early as the first quarter of this century [526], but they did not become popular and remained a means only of qualitative evaluation. The problem in developing an air-based caloric test involved replacing the liquid with air, which has entirely different physical constants. It required entirely different conditions, which could be selected only by taking a nystagmometric approach [147]. Exposure temperatures and time were set so that cold and warm nystagmi of equal intensity could be produced. And there is another example. During study of optokinetic reactions under various experimental conditions, only careful quantitative evaluation of nystagmus parameters made it possible to determine the actual feasibility of producing subcortical OKN in a human [119, 122]. Then these results served as the basis for developing a new optokinetic test.

These examples emphasize the idea that a particular technique for studying vestibular function is of real value when the resulting reaction can be quantitatively evaluated and when the regularities by which this reaction forms are known. Nystagmus is one of those reactions which are "convenient" from the standpoint of the researcher. Its quantitative characteristics can give much valuable information on processes in the system

studied. Therefore, nystagmometry plays a vital role in working out optimum procedures for vestibulometric research [117-122, 127-130]. Quantitative evaluation of nystagmus is thus absolutely necessary to solve the following problems: studying the mechanisms of nystagmus itself, identifying vestibular dysfunction, and developing new vestibulometric tests and diagnostic rules.

Chapter 2. Vestibular Nystagmus and Optokinetic Nystagmus /66

Visual-Vestibular Integration and Nystagmometry as an Approach to Its Study

The two analyzing systems -- visual and vestibular -- are quite closely related. Their relationship is reciprocal and rather complex; i.e. it exists on many levels, involves various anatomical-physiological substrata, and is quite diverse in its manifestations.

Under natural conditions, when a healthy organism is not exposed to any unusual forces, the relationship which we are discussing is not apparent and may remain unnoticed, since system interaction is coordinated and there are no reasons for functional disturbances or sensations of discomfort. Given any sort of deviations from coordinated effort, when one or both systems are subjected to unusual forces or develops a pathological condition, the relationship may become more clear precisely because of these disturbances. Therefore, one possible technique, which facilitates identification of this relationship to study it, may be artificial recreation of the conditions which disturb system coordination, promote conflict between the systems, and indicate deviations from the norm. In psychology, these deviations may include, for example, incorrect judgment of reality -- visual illusions resulting from the effect of signals from the vestibular apparatus [71], illusory evaluation of the position of the body in space as a result of altered visual signaling, etc. The relationship between systems becomes outwardly noticeable when changes affect how movements, especially eye movement, are organized.

Vision is hardly possible without ocular motility, i.e. without active participation of extraocular musculature, with its system of motor nuclei and efferent and afferent paths. It is no exaggeration to state that eye movements exist only to ensure normal performance of the visual analyzer [141, 202].

Generally speaking, any assignment which the visual system performs requires coordinated effort of the oculomotor and vestibulo-oculomotor systems, and any lack of coordination (called "conflict") complicates problem-solving or makes it impossible. The concept of conflicts can be illustrated by the following two examples. /67

Optokinetic stimulation can cause motion sickness with all the associated symptoms. As has been discovered, motion sickness symptoms can be significantly weakened if the subject actively turns his head from shoulder to shoulder in the plane in which the optokinetic stimulus is moving [417]. Approaching evaluation of this observation from the standpoint of system coordination, it is natural to suggest that motion sickness caused by an isolated optokinetic stimulus results from a

conflict: signals from the unstimulated vestibular apparatus (rest signal) contradict signals from the stimulated visual system indicating motion. The positive effect of active movements is apparently related to the fact that the vestibular system provides additional information which causesthe illusion of rotation to one side and other symptoms of the illness to be suppressed.

One might cite a different sort of example: observations related howfixed eye versions are accomplished during stimulation of the vestibular apparatus [8]. The subject's assignment was to shift his gaze from one given point to another. This task could not be performed when the vestibular apparatus was stimulated by angular acceleration accompanied by vestibular nystagmus. Fixed versions relate to the level of voluntary (active or deliberate) movements, while nystagmus occurs on the unconditioned reflector level, i.e. this example involves organization of quantitatively heterogenous eye movements. However, the relationship is just as complicated when different nystagmi enter into the interaction.

Vestibulo-optokinetic relationships, first studied by Makh [347], still remain one of the most important and interesting problems of nystagmometry, including applied. A few facts have now been accumulated which indicate that particular structures are involved in producing interaction between the two systems, that optokinetic stimulation and visual fixation affect the vestibular system and vestibular reactions, and that there is an opposite effect, i.e. that the vestibular system influences the visual, etc. This data still requires careful analysis and generalization, but, for the time being, the attempt to systematize it presents significant difficulties. Therefore, we present only certain facts which have a direct or indirect relationship to nystagmi -- both vestibular and optokinetic.

Vestibular nuclei have multimodal neurons which react similarly to both vestibular and optokinetic stimulation by changing their activity level. /68 These neurons, which are unquestionably vestibular in nature yet react to optokinetic stimulation, have been described in various animals -- fish, rabbits, cats, and apes [221, 288, 289, 393, 394, 576, 577], even when the effect of feedback from musculature proprioceptors and other extra-vestibular receptors has been completely eliminated. Nerve elements of vestibular nuclei connected with otolithic organs also react to optokinetic stimulation, as has been observed in experiments on cats swung in parallel motions [286]. Let us discuss other electrophysiological research [495, 565] which involves not OKN, but so-called optical nystagmus, i.e. a reaction caused by discontinuous stimulation of optical paths between the retina and the upper colliculus. Various experiments on guinea pigs have conclusively shown that vestibular nuclei are a necessary link in the mechanism of this type of nystagmus. Similar results were obtained with rabbits [243].

Modern concepts in electrophysiology are thus rather specific: in the vestibular nuclear complex, some of the neurons which are activated by vestibular stimulation can also be activated by an optokinetic stimulus.

The paths along which signals travel from the visual system inlet to vestibular nuclei neurons have not yet been studied in detail. However, impulses from the frontal and occipital parts of the cortex pass through vestibular nuclei toward the anterior longitudinal fascicles [539]. The cerebellum (particularly the flocculus) especially takes part in the visual-vestibular interaction. However its role is not as great as was assumed earlier: the cerebellum is not a mandatory link in transmitting afferent signals on OKS to vestibular nuclei neurons [264, 394, 395, 504].

Observation of neurons whose electrical activity correlates with caloric nystagmus (CN) indicates the effect of the vestibular system on the visual. In some units, activity increases during SC; in others, it is inhibited [571].

There is data which indicates an opposite effect, i.e. that of the visual system on the vestibular. For example, it has been observed that electrical activity in afferent fibers of the lateral semicircular canal of an immobilized goldfish change if an OKS moves into its field of vision: when the OKS moves in the nasal direction, activity increases; when it moves in the opposite direction, it decreases [400].

Vestibulomotor reflexes can be inhibited by visual fixation [390]. Preventing fixation has the opposite effect: a strengthening of post-rotatory nystagmus as a result of eliminating vision has been noted both at the early stages of ontogenesis and in adult animals and humans. Experiments on rabbits without visual apparatus in the embryo period demonstrated a strengthening of two-phase rhythmic head oscillations (head nystagmus) in the plane of rotation [155]. During a caloric test, visual fixation of the environment was fairly clearly pronounced: the latent period was prolonged, the duration of nystagmus reduced [174], and SSC sharply suppressed. Therefore various means which prevent the mechanism of visual fixation are used to increase the intensity of nystagmus in diagnostic tests [269]. At the same time, fixation suppression of CN has turned out to be very important from the standpoint of differential diagnosis: lack of suppression is considered to be a sign that the pathological process is centrally localized [354]. /69

Success in studying the effect of the visual system on VN depends greatly on theoretically substantiated selection of parameters by which reactions are evaluated, since reactions behave quite differently. For example, the relationship between the duration, number of impulses, and frequency of post-rotatory nystagmus and the involvement of vision in healthy

children has been discussed [483]. It has been discovered that nystagmus lasts longer in total darkness than under other conditions. In light without fixation (glasses), as well as with fixation on a red point in darkness, nystagmus lasted longer than during rotation in light, when it is possible to fix one's gaze on one's surroundings; fixation on a point in darkness somewhat slows the reaction as compared to the result of rotation in light without fixation. In contrast, nystagmus frequency was greater in situations accompanied by visual fixation. It has been proposed that there are two mechanisms which inhibit the effect of vision on post-rotatory nystagmus: primary oculomotor (involving visual fixation) and primary oculosensor (without visual fixation).

The result of interaction between vestibular and optokinetic stimulation depends on whether the two stimuli match in sign [387]. Experiments on rabbits, for example, indicate a reciprocal effect [316]. During these experiments, animals were simultaneously subjected to optokinetic stimulation and subthreshold stimulation. Additional sub-threshold stimulation, which by itself could not cause nystagmus, intensified the optokinetic reaction. This has been confirmed in control experiments where vestibular nerves were bilaterally severed, since reactions to the rotation of a cylinder and to the rotation of the animal within a fixed cylinder were indistinguishable. Other studies [152, 341] also demonstrated that eliminating labyrinthine effects inhibits OKN, decreasing its frequency. /70
Labyrinths affect the quality of visual tracking of a target's movement and on tracking processes caused in nerve centers by prolonged optokinetic stimulation [72]. After protracted rotation of a rabbit with eyes open, stable rhythmic activity was preserved in the form of counter-rotation nystagmus which developed in darkness and was opposite in direction (as compared to nystagmus during rotation in light). Additional vestibular stimulation modulated this reaction, intensifying or weakening it depending on whether the direction of this nystagmus matched that of the potential vestibular nystagmus.

There are quite a few studies which confirm the close relationship between these reactions (cf. for example [556]) and indicate that the mechanisms of these reactions have much in common. One might add that it has been proposed that VN and OKN have a common FC center [269], and there is much data which seems to indicate common aspects of these reactions. However, it would be a mistake to assert that VN and OKN reactions are one and the same. First we must remember that, in clinical practice, it is well known that either one of these nystagmi can disappear by itself. In McCabe's experiments [446], OKN remained when VN was absent. At the same time, data is accumulating which indicates that disruption of OKN occurs during Menier's disease and other inner ear pathologies [11, 466]. Some are of the opinion that visual afferentation is a primary factor in optomotor reactions, while vestibular and proprio-

ceptive effects act only to modulate it [218, 385, 386].

In attempting to sum up what has been presented here, we arrive at a somewhat contradictory concept. First, VN and OKN have much in common, but not enough to consider them identical. Second, VN and OKN can exist separately, which would seem to indicate their autonomy. However, each of these nystagmi unquestionably depends on the condition of the system which controls development of the other nystagmus: VN depends on optokinetic; OKN on vestibular.

There is no contradiction if we deny that these nystagmi are independent reactions.

The close functional relationship between vestibular and optokinetic nystagmi is quite natural if we regard vestibular nystagmus as a reaction whose biological purpose amounts to facilitating fixation of the eye on its surroundings during angular acceleration. This idea arises from experimental study of oculomotor reactions in rabbits [74, 75]. Similar conclusions were reached in research on humans whose labyrinth function had been completely eliminated [593]. In these people, OKN /71
was near the norm at low stimulation rates, but at $20^{\circ}\cdot sec^{-1}$ and higher, SSC lagged behind the rate of stimulation. It is interesting that reverse post-optokinetic nystagmus (RPN) occurs in these subjects and, consequently, functioning labyrinths are not required for this phenomenon to occur. V. I. Voyachek's hypothesis of the occurrence of vestibular nystagmus based on OKN is well known. In fact, research on the phylogenetic aspect of nystagmic reactions indicates that VN occurred at later stages of development than did OKN. This is demonstrated particularly by the fact that OKN exists in animals in which the vestibular apparatus is represented only by otocysts, while there are no semicircular canals and, therefore, no VN [316].

In the theoretical sense, the interaction between the two nystagmi is part of a general biological problem of the interaction between sensory systems. The applied aspect is just as important: the need is growing to expand the system of nystagmometric research in otoneurology by incorporating into it tests specially designed for studying VOKN, as well as for more detailed evaluation of OKN [278, 404, 419, 551, 502]. This trend is undoubtedly promising. However, the task is not a simple one. Labyrinth activity levels must differ significantly if OKN is to become asymmetric under the influence of vestibular asymmetry [377]. There are two possible approaches. The first is to develop techniques to identify OKN asymmetry. The second is to develop tests with combined stimulation (vestibulo-optokinetic) and with detailed quantitative analysis of the resulting reactions [119, 122, 138, 170].

Finally, new data on the functional plasticity of relationships between the vestibular and optokinetic systems is also

quite interesting from applied viewpoints [272, 273]. This relationship is particularly expressed by the fact that, acting on one system, one can achieve a rather stable change in reactions in the other. It might be that research evidencing the possibility of significant restructurings in these systems under artificially created stimulation conditions offers opportunities to affect the vestibular function through the visual analyzer for therapeutic purposes.

If labyrinths are involved even indirectly in OKN mechanisms, a different type of labyrinth pathology would seem to be reflected. Moreover, as strange as it seems, there is no consistent opinion on this question, since experimental data is contradictory. For example, it has been confirmed that even severing the eighth pair of cranial nerves or destroying the labyrinth has no effect on OKN (cf. [269]). At the same time many facts, in contrast, indicate that OKN depends significantly on the vestibular system's condition [9]. There have been studies in which a bilateral labyrinthectomy changes OKN and suppresses post-OKN [271, 568, 569], while cutting off the vestibular nuclei leads to the disappearance of OKN [229] /72
and modifies cerebral and mesencephalic nystagmi [439], altering the eye's plane of movement.

The source of the contradictory conclusions is apparently the variety of approaches to evaluating experimental nystagmographic materials and the different levels of information provided by quantitative characteristics of nystagmus used to compare reactions.

It has now been shown that nystagmus (both VN and OKN) development involves several different mechanisms which are responsible for particular reaction features [200]. Despite the fact that we know little about these mechanisms, their meaning in terms of an organism, or the ways in which they function, the fact that they exist is unquestioned. Experimental and clinical practice has shown that changes in nystagmus rarely affect only one characteristic or one reaction feature, while remaining properties are unchanged. The most interesting of these mechanisms, which exist in parallel and independently of one another, from the practical (or diagnostic) standpoint are mechanisms which control SSC and reaction rhythm.

In identifying the relationships between OKN and VN systems it is absolutely necessary to be guided by SSC evaluation, since a change in SSC can be quite indicative. However, in experiments studying SSC in animals, we encounter methodological problems related to ENG calibration, which has already been discussed in detail. We can use information on the average calibration factor to obtain additional data on the effect of the vestibular system on OKN. In one study on rabbits [152], OKN ENG's were recorded at an OKS speed of $15^{\circ} \cdot sec^{-1}$; average amplitudes (mkV) and frequencies (sec^{-1}) were calcula-

ted. Then both labyrinths were destroyed and rotatory tests were used to ensure that there was no VN. OKN was again studied. The basic result was that labyrinthectomy definitely decreases OKN frequency statistically, but amplitude does not change. OKN does not return to its initial level, even 6 months later. The amplitudes (in mkV) used can be expressed in degrees, and then, by calculating the product of average amplitude in degrees times average frequency, a value close to SSC is obtained on the angular velocity scale [481]. The result of this additional evaluation of numerical material shows that the OKN SSC of an untreated rabbit averaged $5.6^{\circ}\cdot sec^{-1}$, while labyrinthectomy reduced it to $1.8^{\circ}\cdot sec^{-1}$, i.e. by about two-thirds. Thus, bilateral labyrinthectomy resulted in obvious changes in OKN activity, expressed not only by a reduction in rhythm, but also in a substantial decrease in SSC.

Another study on the effect of labyrinthectomy on OKN in a /73
rabbit [341] indicates approximately the same result: a bilateral labyrinthectomy is accompanied by substantial reduction in OKN frequency. In contrast to research cited previously [152], nystagmus was recorded over a wide range of OKS angular velocities ($20\text{-}150^{\circ}\cdot sec^{-1}$) in both control and test animals. This made it possible to obtain a curve for nystagmus frequency as a function of stimulus. In untreated rabbits, the curve was bell-shaped with maximum around $50^{\circ}\cdot sec^{-1}$. The typical shape of the curve was preserved even after labyrinthectomy and the maximum remained at the previous level on the stimulus scale. There was a dramatic decrease in frequency (from 65 impulses per minute in untreated rabbits to 13 after the operation, i.e. by a factor of five).

After these examples, there is no doubt that OKN in a rabbit is strongly affected by the vestibular system. However, we must emphasize that bilateral disconnection of the labyrinths took place in both studies. Moreover, applied work requires an understanding of the changes which can occur in OKN if labyrinth activity changes asymmetrically.

A phenomenon well-known in otoneurology can serve as an example to confirm the relationship between systems if vestibular function is asymmetrical: OKN in one direction predominates over OKN in another in neurinoma of the eighth nerve [64]. Otoneurologists believe that this symptom is a clear sign that a tumor is localized near the vestibular nuclear complex, rejecting the possibility of OKN asymmetry with distal tumor localization. This viewpoint is based on a large of number of clinical studies. However, several experimental findings warn against being too categorical in this area. For example, in experiments on cats, a month after unilateral labyrinth removal it was observed that (1) OKN generally became less intense, and (2) OKN caused by movement of the stimulus from the untreated to the treated side was the weakest.

The diversity of opinions on the relationship between OKN and peripheral networks in the vestibular system can be explained in several ways. One cause may be a certain dissimilarity in OKN mechanisms in different biological subjects. Another cause relates to the fact that clinical research is often done without detailed quantitative evaluation of nystagmographic material. Still another reason could be the hypotheses underlying a great deal of applied nystagmometric research -- particularly the concept of the biological role of VN. This last reason is quite important and merits further discussion.

As already noted, eye motility exists ultimately because it takes part in the function of vision, but, at the same time, vision is not a mandatory condition for eye motion. Eye movement during sleep is a common example of independent, i.e. unrelated to vision, motor activity. Involuntary activity of the oculomotor system can be considered another such example. This system is a necessary component of another more complex system which produces vision. The oculomotor system in turn consists of several simpler components which are involved in organizing particular types of eye movement (drifting, tracking movements, jumping et al.). If vision is eliminated, eye movements can be organized and strictly ordered. Such reactions include vestibular ocular nystagmus. VN does not require vision -- it can occur with eyes closed, in darkness, in the blind, etc. VN exists even in those whose vision never functioned [155]. /74

These facts, which seem to demonstrate that there is no direct relationship between VN and the vision system, and that its occurrence requires several unusual conditions (action of rather prolonged high angular acceleration), have given several authors reason to consider VN not as a physiological reaction, but as one closer to pathological, without biological meaning [389]. From this viewpoint, VN is interesting only as a "convenient" reflex for diagnostic purposes, for experts evaluating vestibular function, etc.

However, several facts seriously contradict this point of view. First, VN occurs without exception in all animals studied so far, i.e. this reaction is preserved (and, according to some information, refined) in phylogenesis. Second, VN, like other organism functions whose biological value is unquestioned, proceeds through several consecutive phases (tonic deviation, mild oscillations, pronounced nystagmus, increased excitement, et al.), depending on the individual animal's development. In other words, this reaction is developed in ontogenesis [96, 155, 555]. Third, VN is structured according to a rather complex program which comes about with participation of various mechanisms [113, 270]. It is assumed that there are five such mechanisms [200, 202], but certain data indicates that there are more (they control nystagmus direction and plane; rhythm, rate, and duration of individual components; and the relation-

ship between components).

Vestibular nystagmus is thus a rather complex reaction, reliably preserved in phylogenesis and naturally developing in ontogenesis. It is hardly likely that a reaction without biological meaning could have these qualities. In other words, there is reason to consider the existence of a special system which brings about VN. Naturally, the question immediately arises as to why this system is needed. To answer briefly, it is needed to work together with the optokinetic system. The hypothesis [74, 75] can be presented in somewhat more detail in the form of the following three theses. /75

1. Both vestibular and optokinetic nystagmus are only elements, parts of a certain complex and singularly biologically useful reaction: vestibulo-optokinetic nystagmus. Mechanisms of both nystagmi, operating harmoniously as subsystems, take part in bringing it about. The system of vestibulo-optokinetic nystagmus is based on these subsystems.

Note that the term "system" here and henceforth is used as a rather general means to identify not only particular morphological substrata, but so-called mechanisms as well, i.e. functional relationships between these substrata in the development of the reaction; or, more precisely, laws to which the physiological processes of such substrata (such as inhibition, excitation, etc.) are subject.

2. The interaction of the two systems (as subsystems) is more than just the simple sum of two nystagmic processes occurring in parallel at a common output element -- the eyeball with its extraocular musculature. The final result of the interaction is determined by significant subsystem functions. These are not defined once and for all. Depending on the specific conditions under which the interaction takes place, they can vary according to the way in which the subsystems' functional capacities change.

Let us introduce a fact to illustate this thesis. The optokinetic system acted upon simultaneously by the vestibular (subthreshold for the last stimulus) can generate optokinetic nystagmus over a wider range of OKS rates than when optokinetic stimulation is isolated [316].

3. Each reaction which takes place separately (i.e. optokinetic nystagmus and vestibular nystagmus) should, to a certain extent, be considered an inferior reaction, since, during reaction formation, the entire vestibulo-optokinetic system operates without information: in the first case, vestibular, in the second visual.

In other words, vestibular nystagmus (e.g. the reaction to accelerated clockwise rotation in a horizontal plane in dark-

ness) should be regarded as a reaction to a certain moderately conflicting situation. The conflict results from lack of information. The vestibular system signals the unified vestibulo-optokinetic system about accelerated rotation, its direction and plane, while the visual system provides no signals similar in content, i.e. it does not confirm the correctness of the arriving signals. /76

The next step in this concept is the assumption of interaction when a conflict situation develops when information from one or both systems is known to be false. Here we can imagine a series of alternatives beginning from a moderate discrepancy in information, when both systems signal rotation in the same plane and in the same direction, and ending with much more acute conflicts when subsystems signal that motion is occurring in different directions or planes.

The simplest example is the nystagmic reaction occurring during rotation with eyes open in light under the influence of negative angular acceleration, when vision provides correct information on inhibition of rotation in one direction, while the vestibular apparatus signals that a change in rotation direction is occurring.

The reaction occurring during positive angular acceleration in light (if the visible surroundings are immobile) can be considered a result from coordinated subsystem activity. However, this does not mean that the subsystems are equally involved under all conditions. There is data, for example, which indicates that the optokinetic system is rather inert, in any case as compared with the vestibular system. This forces us to assume that its role in reaction formation during accelerated rotation in light will be less important than that of the vestibular system.

Nystagmus with Combined Vestibular and Optokinetic Stimuli in a Physiological Experiment

If these assumptions are valid, we should expect that analysis of nystagmus caused by combined stimulation will make it possible to identify reaction features which cannot result from the simple addition of two nystagmi.

This has been shown in research on rabbits [74, 75]. The vestibular apparatus was stimulated with a programmable stand. Trapezoidal stimulus with positive and negative accelerations of equal magnitude ($6.0^{\circ}\cdot sec^{-1}$ over 5 sec) were used. Rotation at a constant speed of $30^{\circ}\cdot sec^{-1}$ lasted 2 min. Tests were made in darkness and/or in light.

Optokinetic stimulation was achieved in two ways. In the first the animal was rotated on a stand at constant angular velocity ($30^{\circ}\cdot sec^{-1}$) in the center of an illuminated prism of white panels with black vertical stripes. This simulation of an /77

optokinetic cylinder is 250 cm high and measures 292 cm from face to face. There are a total of 24 black stripes, each 7 cm wide. Light sources were arranged on the stand and rotated along with the animal. Therefore illumination of the field of vision for each eye during rotation remained constant. A bench with a head-turning device was used to keep the animal fixed. The head was oriented so that the axis of rotation passed between the labyrinth and the lateral semicircular canals lay in the plane of rotation. In the second part of the experiment, which took place on another stand, OKN was produced in an immobilized animal in the center of a rotating optokinetic cylinder whose dimensions correspond to those of the prism described above. Combined stimulation of vestibular and optokinetic systems was achieved by accelerated (or slowed) rotation of the rabbit, i.e. by a trapezoidal test conducted in an illuminated prism. Oculomotor reactions were recorded by electronystagmography. Direct calibration [22-24] was usually done twice: before the experiment and immediately upon its completion. When, during the experiment, the animal was alternately subjected to darkness and then to light, calibration was repeated to prevent error in evaluating ENG's, which could occur due to changes in corneoretinal potential.

The material underwent primary processing (examples of ENG's are shown in figure 26) by hand. Then tables of dynamic characteristics and their individual and combined graphs were produced.[1] Figure 27 shows the result of this combination. Student's criterion and the non-parametric criterion [2] were used for statistical evaluation. In the description of the results below we will use the following concepts: Vestibular nystagmus (VN) -- the reaction caused by an experimental vestibular test without involvement of vision. It can be rotatory (VVN -- reaction to positive angular acceleration) or post-rotatory (VPN -- with negative angular acceleration); Optokinetic nystagmus (OKN) -- the reaction caused without direct involvement of the vestibular system in response to the movement of objects in the field of vision. OKN can be caused by movement of visual stimuli relative to the immobile head or by rotation of the subject with a certain angular velocity relative to the immobile surroundings; Vestibulo-optokinetic nystagmus (VOKN) -- the reaction caused by the combination of stimuli (vestibular and optokinetic). If stimulation is coordinated (matching in sign), it is called coincident vestibulo-optokinetic nystagmus (VOKNC); if it is uncoordinated -- noncoincident vestibulo-optokinetic nystagmus (VOKNN).

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1 Characteristics are discussed in detail in chapter 3.

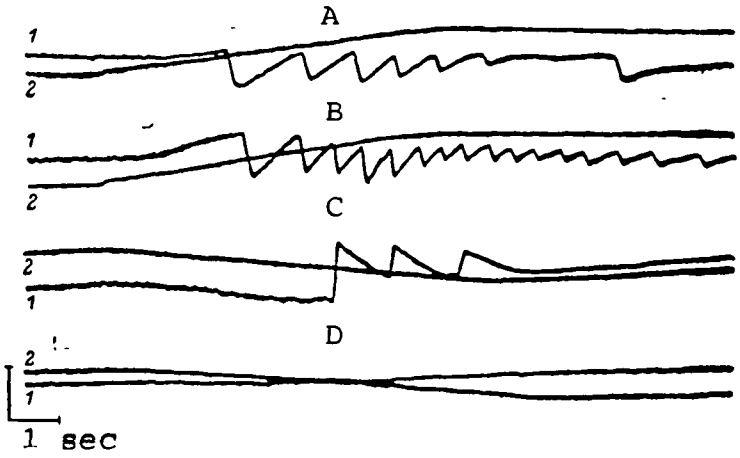

Figure 26. Electronystagmogram of a rabbit during positive (A and B) and negative (C and D) angular accelerations when rotated in darkness (A and B) and in light (C and D) (from [75]).

1 -- ENG; 2 -- Stand rotation speed; A -- VVN (optokinetic system not directly involved in formation of nystagmus); B -- VOKNC (concomitant involvement of vestibular and optokinetic systems, coincidence of stimuli in terms of magnitude and sign); C -- VPN (no direct involvement of the optokinetic system); D -- total inhibition of post-rotatory reaction (antagonistic effect of the optokinetic system). Calibration: 1 mV, 1 sec.

The goal of the experiments was to determine whether and how VOKN and VN differ (particularly VOKNC and VVN; VOKNN and VPN). The following assumptions were used as a basis. If there is a difference, then it is natural to consider it to be the result only of involvement of vision, since vestibular systems are identical. If the differences in the first and second pairs are identical, then the discrepancy may be caused by the difference in vestibular stimulation (acceleration, inhibition), as well as by more complex factors inherent in the specific nature of the combination of effects of optokinetic and vestibular stimulation. Therefore, one particular task was to check how similar or different were vestibular reactions to positive and negative acceleration in a rabbit.

The following characteristics were used for comparison: latent period (LP, msec), reaction duration (DR, msec), frequency at the dynamic characteristic extremum (F, sec^{-1}), slow component speed at the extremum (SSC, $^{\circ}\cdot sec^{-1}$), duration of the slow component (DSC, msec). Evaluation in terms of these characteristics by manual processing of ENG's was preceded by: plotting dynamic characteristics, finding the extremum, statistical evaluation of the location of the extremum on the time

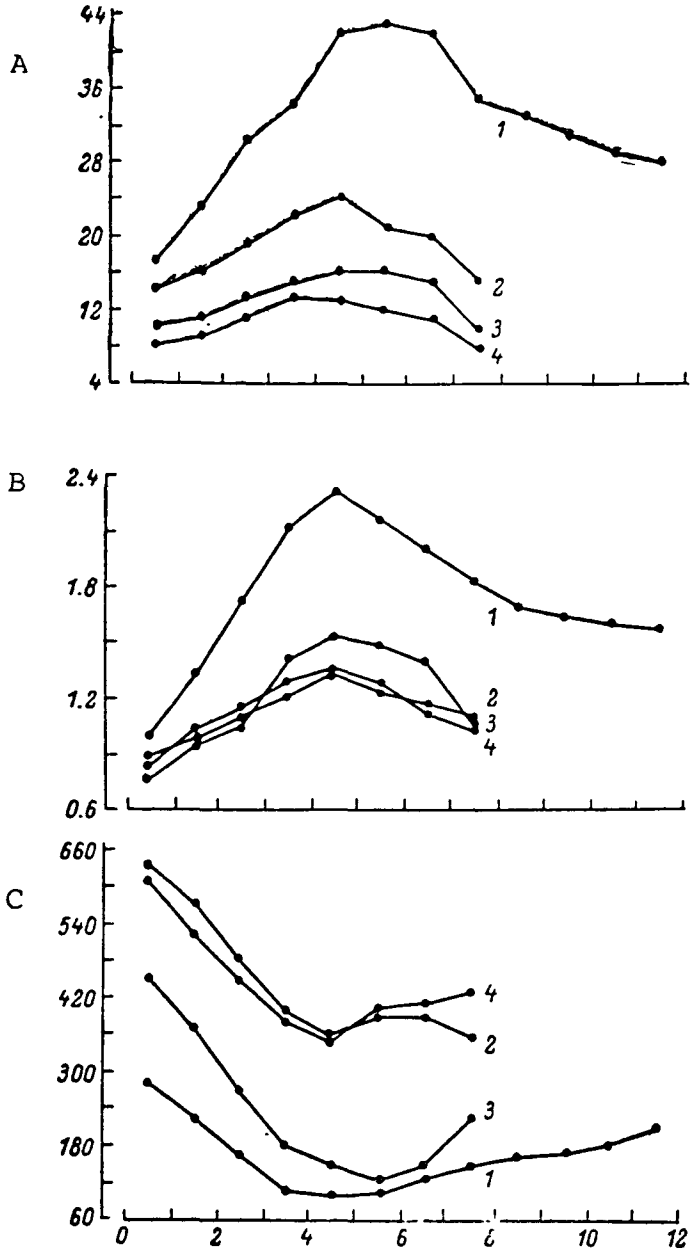

Figure 27. SSC, frequency and DSC of nystagmic reactions in a rabbit as a function of stimulation conditions (as per [75]).

X-axis -- time, sec; Y-axis -- (A) SSC, °·sec^{-1}; (B) F, sec^{-1}; (C) DSC. msec; dynamic characteristics were obtained by averaging 12 ENG samples at 1-sec intervals. 1 -- VOKNC; 2 -- VVN; 3 -- VOKNN; 4 -- VPN.

axis and of the most extreme values of dynamic characteristics in absolute values. All ENG's were subjected to evaluation in terms of duration, regardless of their quality. During evaluation in terms of other characteristics, the scope of the sample depended on the ability to process ENG's in detail, about which

comments are made at the appropriate points.

Comparison in Terms of Duration. All ENG's were broken down into three categories: O - no rhythmic reaction; M - nystagmus curtailed when constant angular velocity is achieved or somewhat earlier; B - nystagmus which lasts longer than the effect of acceleration. Reaction inhibition, completely absent in VVN and VOKNC, was frequent in the VOKNN sample; among the latter, more than one-third were of category O. The four types of reaction were compared in terms of criterion χ^2 (frequency of a particular indicator was evaluated). At this stage in processing, the basic result (table 3) amounted to the following: if vision is involved in the formation of post-rotatory nystagmus, the probability that the reaction will be completely inhibited increases decisively.

TABLE 3
DISTRIBUTION OF ENG'S IN TERMS OF DURATION

ENG category	Positive Acceleration		Negative Acceleration		Total
	Dark VVN	Light VOKNC	Dark VNN	Light VOKNN	
O	-	-	1	15	16
M	1	5	3	8	17
B	21	40	23	17	101
Total	22	45	27	40	134

*NOTES: 1. The difference in VNN and VOKN samples is certain in terms of probability of complete nystagmus inhibition (category O) ($\chi^2 = 10.128$). 2. The difference in VVN and VOKNC samples in terms of reaction duration greater than 6 sec (category M) is not certain ($\chi^2 = 0.781$).

Comparison in Terms of Other Characteristics. ENG's selected were those in which latent period (LP) -- the period from the beginning of the effects of angular acceleration until the beginning of the SC of the first nystagmic impulse, as well as reaction duration (DR) -- the time from the beginning of SC until the end of the next FC could be calculated with certainty. In addition, total duration (TD) was calculated as the sum of LP and DR.

Table 4 presents the results of statistical processing. The results for the comparison in terms of time (Student's criterion was used) are: VVN and VPN do not differ significantly; VOKNC and VOKNN differ substantially in terms of DR and TD (the second has fewer characteristics); their difference in terms of LP was close to certain; VVN and VOKNC definitely dif-

fered in terms of all time characteristics; VPN and VOKNN did not./81

Note, however, that the difference in VPN and VOKNN in terms of time characteristics cannot be completely denied, since, first, the discrepancy between these two types of reaction was clear during qualitative evaluation in terms of inhibition and, second, during ENG sampling, as we noted earlier, sharply inhibited reactions and all those in category 0 were eliminated from the sample (DR could not be evaluated for them).

Table 5 shows a comparison in terms of frequency, SSC, and DSC.

The primary results of this analysis are summed up as follows. VVN and VPN are indistinguishable in terms of quantitative characteristics. Actually, these reactions are not independent types. VOKNC differs substantially from VVN. This discrepancy is basically quantitative: VOKNC has greater duration, frequency maximum, and SSC maximum. VOKNC differs substantially from VOKNN. The difference is also quantitative. VOKNN and VPN differ in that the first has a higher probability of inhibition, i.e. curtailed reaction or even complete lack of rhythmic activity. At the same time no definite difference between the averages for frequency maximum and SSC samples could be observed.

The effect of the visual system's involvement in nystagmus development depends on the sign with which the optic inlet participates in reaction formation: if signs match, the reaction is intensified; if they do not match, it is weakened.

Further, two series of experiments were conducted to find OKN characteristics under conditions in which involvement of the vestibular apparatus is minimized. The task of the first series was to find the time required for OKN to reach greatest activity. This was determined according to when highest nystagmus frequency occurred. In experiments in this series the animal was not subjected to rotation, but the optokinetic cylinder rotated around him at a rate of $36^{\circ} \cdot sec^{-1}$. Experiments were set up under conditions of adaptation to light. Optokinetic stimulation was eliminated immediately by covering the subject's head with a screen which allow light to pass through, but did not permit observation of a black and white drawing on the inner wall of the cylinder. When the EOG was switched on, the screen was removed and recording continued for 20 min. Table 6 presents the results of evaluating OKN (260 nystagmic impulses were processed). The average frequency at the extremum for all ENG's was close to 0.5 sec^{-1}. Several tenths of a second were required to reach maximum frequency in each case. OKN latent period in these experiments was from 1.5 to 4.0 sec.

The object of the second series of experiments was to find average OKN SSC when the animal was rotated at constant angular velocity of $30^{\circ} \cdot sec^{-1}$. The rabbit lay in a rotating stand

TABLE 4 /82
TIME CHARACTERISTICS (LP, DR, TD)
IN NYSTAGMIC REACTIONS OF VARIOUS TYPES ($\bar{x} + \sigma$ IN MSEC)

Reaction Characteristic	Type of Reaction VVN (1)	VPN (2)	VOKNC (3)	VOKNN(4)	P_{1-2}	P_{2-4}	P_{1-3}	P_{2-4}
LP	1484.2±182.3	1126.5±109.1	1091.8±74.5	868.5±74.0	0.10	0.05	0.02	0.10
DR	7177.1±496.5	7189.1±382.8	15552.3±2382.9	7127.6±403.1	0.80	0.01	0.01	0.90
TD	8661.4±15.2	8316±372.7	16643.9±2378.3	7968.5±393.0	0.50	0.01	0.01	0.50
Total ENG's	21	23	38	21				

NOTE: $\bar{x}$ is arithmetic mean; σ - root-mean-square deviation; P - probability of error during negation given affiliation to one set.

TABLE 5
COMPARISON OF NYSTAGMOMETRIC CHARACTERISTICS IN FOUR SAMPLES

Characteristic	Stimulus Conditions	Acceleration Positive(3)	Acceleration Negative(4)	P_{3-4}
Frequency*	Dark (1)	1.45±0.05	1.45±0.04	>0.05
	Light (2)	2.54±0.02	1.73±0.08	<0.05
	P_{1-2}	<0.05	>0.05	
SSC*	Dark (1)	19.80±4.98	11.34±2.79	>0.05
	Light (2)	38.16±5.58	14.73±2.19	<0.05
	P_{1-2}	<0.05	>0.05	
DSC**	Dark (1)	718±82	666±72	>0.05
	Light (2)	345±28	506±23	<0.05
	P_{1-2}	<0.05	>0.05	

*Average maximum for sample and its error, sec^{-1}
**Average minimum for sample and its error, msec.

within an immobile optokinetic prism. Experiment conditions differed from those of the main experiment on studying VOKNC only in that the initial angular acceleration had no effect whatsoever on the reaction. The use of direct calibration made it possible to find the desired characteristic in units of angular velocity. Average OKN SSC under these conditions equaled $28.5 \pm 4.8^{\circ} \cdot sec^{-1}$, i.e. close to rotation speed. /83

TABLE 6
RESULTS OF EVALUATING 9 OKN ENG'S RECORDED IN THREE RABBITS

Rabbit Number	Number of Nystagmic Impulses Evaluated	Maximum Frequency sec^{-1}	Time to Reach Maximum, sec
1	30	0.51	18
1	30	0.45	46
1	30	0.41	11
2	30	0.52	54
2	30	0.51	68
2	30	0.45	10
3	30	0.82	10
3	25	0.33	80
3	25	0.12	70
	$\bar{x} \pm m$	0.46 ± 0.06	40.17 ± 9.6

Table 7 compares OKN characteristics with two other reactions -- vestibular and vestibulo-optokinetic.

TABLE 7
COMPARISON OF CHARACTERISTICS IN THREE TYPES OF NYSTAGMIC REACTIONS ($\bar{x} \pm m$)

Reaction Type	SSC, $^{\circ} \times sec^{-1}$	Maximum Frequency, sec^{-1}	Time to Reach Maximum Frequency, sec	Latent Period, msec
VVN(1)	19.8 ± 4.98	1.45 ± 0.05	4.350 ± 0.426	543 ± 182
OKN(2)	28.5 ± 2.79	0.46 ± 0.06	40.770 ± 9.600	2404 ± 648
VOKNC(3)	38.1 ± 5.58	2.54 ± 0.02	2.759 ± 0.326	150 ± 74
P_{1-2}	>0.05	<0.05	<0.05	<0.05
P_{1-3}	<0.05	<0.05	>0.05	<0.05
P_{2-3}	>0.05	<0.05	<0.05	<0.05

NOTES: 1. OKN SSC was calculated from results of experiments on two animals. 2. Frequencies for VVN and VOKNC were calculated as the average of individual maxima with the animal rotating at $6^{\circ} \cdot sec^{-1}$ for 5 sec; for OKN - at constant optokinetic cylinder rotation speed ($36^{\circ} \cdot sec^{-1}$) around an immobile animal.

Noteworthy here are both the difference in frequencies and SSC's and the fact that, with combined vestibulo-optokinetic stimulation, the time required for the nystagmus to achieve maximum activity was less than the duration of the effect of angular acceleration, i.e. gradually intensifying VOKNC reaches /84

a certain limit before the stand shifts to rotation at constant velocity.

We have already presented facts which demonstrate that additional vestibular afferentation increases optokinetic system activity. There are several other similar indications. For example, it has been observed that OKN occurs with a smaller LP, while its frequency increases if angular rotation in darkness, i.e. vestibular stimulation, precedes optokinetic stimulation. This effect has been explained by the phenomenon of "itineration." It has been proposed that optokinetic stimulation is somehow superimposed on an existing path left in the centers after vestibular nystagmus [248]. After information on the behavior of multimodal neurons in vestibular nuclei was obtained ([276] et al.), one might have thought that this effect is determined by switching these neurons from one afferent signal to another. Note another study [270] which established that OKN SSC in rabbits does not reach maximum immediately, but rather gradually, and the time this takes depends on stimulus movement speed. This time varies from 1 sec to 1 min (given a range of optokinetic stimulus speeds from 1 to 30.5°·$\cdot sec^{-1}$). OKN SSC always lags a little behind stimulus speed.

Experiments on rabbits [75, 131] revealed that after VOKNC there is often a pause during which the eye remains stationary (cf. figure 28). Only after a certain time (if rotation at constant angular velocity is not stopped) does OKN develop gradually. When there was no pause, i.e. VOKNC shifted directly to OKN, dynamic characteristics where this shift occurred always diminished somewhat (cf. figures 27, 29), as if to indicate that OKN develops gradually and independently of VOKNC.

All this justifies the statement that a rabbit's optokinetic system is characterized by rather substantial inertness.

Thus the thesis that simple algebraic summation of two afferentations is the cause of the difference in VOKNC and VVN is not proven.

VOKNC derives from an LP which is shorter than both OKN and VVN. Small LP is an essentially new feature which differentiates this reaction from its components.

VOKNC is distinguished by very high frequency. Its frequency is five times higher than that of OKN and twice that of VVN. This is also a new feature which cannot be explained by simple summation.

VOKNC has an SSC quite close to the animal's momentary rotating speed relative to the immobile surroundings, sometimes even exceeding that speed. Neither VVN nor OKN exhibits this characteristic.

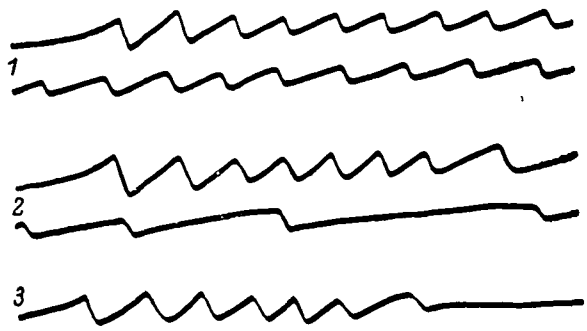

Figure 28. Three forms of transition from VOKNC to OKN when a rabbit is rotated in light (as per [131]).

1 -- Direct shift from VOKNC to prolonged, stable OKN; 2 -- An area of nystagmus with slow rhythm and reduced SSC exists between VOKNC and OKN; 3 -- After VOKNC there is a definite pause and OKN develops only after several tenths of a second after rotation begins. On ENG's 1 and 2, the bottom line is a continuation of the recording.

Purely vestibular nystagmus does not permit tracking motion speed, since there is no visual monitoring or feedback. OKN in a rabbit (i.e. the reaction which occurs when there is feed- /85

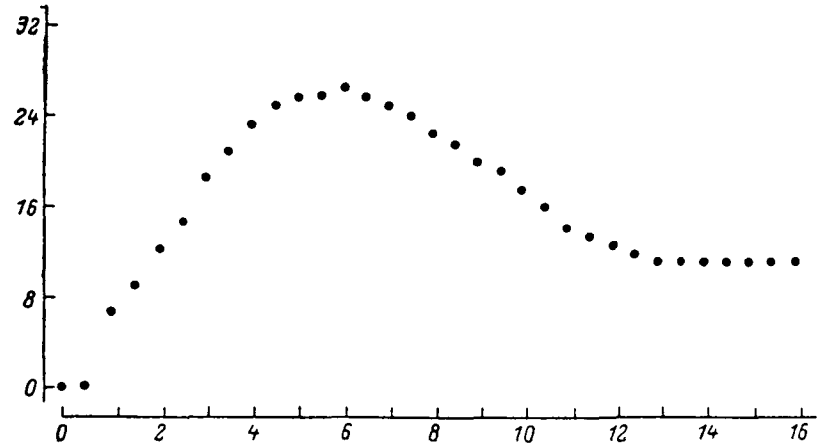

Figure 29. Dynamic characteristic plotted from VOKNC ENG's.

X-axis -- time from onset of stimulation, sec; Y-axis --SSC, $^{\circ}\cdot sec^{-1}$. The graph was produced by computer processing of the average SSC for each interval (0.5 sec) and leveling the curve by sliding weighted average method. The area in which the reaction weakens after the effect of angular acceleration has ceased is clearly visible.

back) is also not appropriate for fulfilling this task, especially when stimulus speed changes over short periods of time because the optokinetic system is characterized by inertness. The two systems must interact to fix an immobile image of the surroundings on the retina. Given this interaction, visual feedback ensures more precise correspondence between eye motion and stimulus speeds, while vestibular system mobility frees the reaction from the inertness typical of the optokinetic system. /86

As compared with VVN and OKN, VOKNC is thus a qualitatively different reaction, combining only certain properties typical of each individual nystagmus and offering certain advantages in the biological sense. VOKNC cannot be considered to be optokinetic nystagmus modified by the involvement of vestibular afferentation. There is no reason to think that VOKNC is a vestibular nystagmus only somewhat corrected by additional optokinetic stimulation. The significant shortening of the reaction's LP when the two systems are involved in reaction development is an unquestionable sign of a low threshold. However, this is not the lowered threshold of the vestibular system, but the threshold of a complex vestibulo-optokinetic system responsible for VOKNC.

The two afferentations are, of course, integrated, and this integration always occurs with regard for signs. However, simple algebraic summation cannot explain cases when, for example, the LP in VOKNN, which is generally characterized by inhibition, is shorter that that of VPN.

Deciphering the mechanisms by which nystagmus occurs during vestibulo-optokinetic stimulation is hardly possible without using electrophysiological data which is now being rather actively collected. Naturally, there is a great deal of interest in experiments directly devoted to the study of vestibular nucleus neuron activity during vestibular, optokinetic, and vestibulo-optokinetic stimulation [574-577]. Vestibular nucleus neurons in apes behave differently under these three stimulation conditions [574]. Positive acceleration of the optokinetic stimulus is accompanied by increased discharge frequency, which is restricted by a certain level of saturation. The level of saturation is always somewhat behind the level of activity of which the neuron is capable during vestibular stimulation (comparison with stimuli similar in velocity profile), while saturation is somewhat delayed in relation to the point at which when the optokinetic stimulus achieves constant velocity. Saturation has been observed at an OKS of $60^{\circ}\cdot sec^{-1}$ and further increase in stimulus velocity does not cause activity to rise. If stimulus angular velocity drops, vestibular nucleus multimodal neuron discharge frequency decreases after velocity has reached $40^{\circ}\cdot sec^{-1}$. Coordinated vestibulo-optokinetic stimulation produces an effect quite similar to that of isolated vestibular stimulation. If vestibulo-optokinetic stimulation is not coordinated, some

neurons exhibit abrupt decreases in activity which, after a certain time, can be below the level of spontaneous activity at rest. These facts are very important in understanding the reasons for the significant differences observed during nystagmometric comparison of VOKNC and VOKNN. /87

Despite the existence of features unquestionably common to vestibular and optokinetic nystagmus, these reactions are not identical as is sometimes stated [556]. However, the result of the interaction of these two systems can rightly be considered not as the simple sum of the two reactions, not as one of them merely intensified or weakened by the influence of the other [248], but as a qualititatively unique reaction, which under ordinary conditions is mostly responsible for providing a fixed image of the surroundings on the ocular retina. If interaction is coordinated, each system involved in causing the reaction makes its contribution: the vestibular system makes it possible to track a quickly changing stimulus (by changing in speed) and the optokinetic to correct eye movement speed, increasing the accuracy of this tracking. The integrated reaction -- VOKNC -- is organized by a rather complex system which in turn consists of two subsystems -- vestibular and optokinetic. Each of these is autonomous in the sense that its activation does not require mandatory coordinated participation of the other system. For example, one vestibular stimulus is adequate to bring about VN, but this does not mean that the optokinetic system remains uninvolved. In any case the entire vestibulo-optokinetic system is functioning. Figuratively speaking, vestibular nystagmus mechanisms exist for each other's sake and because, at any moment, they may be needed for the development of VOKNC. These mechanisms, with their characteristic automatism, bring about VN every time, even in response to a purely vestibular stimulus, i.e. even when vision is prevented (e.g. during rotation in darkness) or when the surroundings are fixed relative to the subject (e.g. during a caloric test). Apparently, VN is organized each time with involvement of the entire vestibulo-optokinetic system, while the ultimate effect depends on the level of coordination of optokinetic system and vestibular system afferentation.

This information, as well as several studies [7, 373, 557] devoted to oculomotor reactions during combined stimulation, can be regarded as the basis for developing essentially new vestibular tests. The object of study in these tests is the condition of the mechanisms by which the vestibular and optokinetic systems interact as subsystems involved in formation of a biologically expedient reaction -- vestibulo-optokinetic nystagmus.

Schematically, one possible alternative test is that consisting of the following components: study of VN; study of OKN; study of VOKN -- reactions to combined vestibulo-optokinetic stimulation; comparison of these three forms of reactions obtained in one subject, quantitative evaluation of their rela- /88

tionship, comparison of the latter with data obtained for the norm. There is much that remains unclear in this very general schematic.

Although the initial stage of this proposed plan can be considered ordinary and necessarily occurring in each vestibular complex, this is not true of the second stage, since techniques for objective evaluation of OKN symmetricity are not well enough developed and without this we cannot evaluate VOKN. Several articles have been devoted to this problem [138, 190].

A primary obstacle in studying VOKN is the fact that OKN in humans is a reaction which is to a large extent cortical, while monitoring it at the cortex inevitably show up both in nystagmometric characteristics of OKN and in the development VOKN. Therefore, the question whether a subcortical form of OKN exists in man must be answered. This form apparently must be considered a component in VOKN development.

Finally, we must be sure that vestibular afferentation can affect OKN characteristics to the extent that a reaction obtained during vestibular stimulation carried out during optokinetic nystagmus can be selected as a VOKN [139]. These questions are discussed below in detail.

Optokinetic Nystagmus in the Norm

The norm for OKN has been studied in children [138, 190]. All were subjected to careful otorhinolaryngological laboratory examination beforehand and were included in the test group only if they had favorable otiatric, ophthalmological, and neurological histories and if the otoscopic picture was normal. Children were selected for the test on the basis of the following considerations. First, the norm for OKN was of interest in and of itself, since it is required for diagnostic research. Second, it was possible to assume that OKN in children has certain qualitative peculiarities as compared to reactions in adults, since traditional methods usually used to study OKN in a clinic could not provide stable enough reactions. A special technique had to be developed.

Sufficiently stable optokinetic reactions in children from 3 years of age could not be produced by replacing the traditional "striped" drawing with a "spotted" one. Round white spots (7°) on a dark field were projected on a screen which occupied most of the field of vision (120° x 70°). A diaprojector projected the drawing. Black movie film with random round holes traveled through the film track of this projector /89
by means of a separate film-winder. The angular velocities at which the drawing traveled were 4.10 and $20^{\circ} \cdot sec^{-1}$. Large screen dimensions minimized the effect of the surrounding immobile objects, while the lack of drawing uniformity -- white spots on a black field -- promoted OKN. No instructions were

required before the research. After 10-minute of adjustment to dim lighting, calibration was done, showing topical drawings with an angular distance of 20° between them on the screen.

Electronystagmographic material (234 ENG's) was obtained during observation of 39 children aged 3 to 7. Recordings were made for each child as the stimulus moved from left to right and from right to left in a horizontal plane. The ENG's were recorded using cutaneous metal electrodes on the outside corners of the eye sockets, a biopotential amplifier, and a self-recording printer. For each ENG, a 20-sec section of the reaction was processed by measuring elementary characteristics (cf. chapter 3) at each nystagmic impulse. Average amplitude was found with regard for the calibration factor. The number of impulses in the same OKN segment was calculated to determine average frequency. The product of average amplitude and average frequency was considered equivalent to OKN SSC.[1].

Physiological asymmetry was taken as the ratio of the difference between the SSC's of reactions different in direction from their sum: $(OKN_r\ SSC - OKN_l\ SSC)/(OKN_r\ SSC + OKN_l\ SSC)$.

Table 8 present the basic results of statistical processing performed according to the traditional description of the norm in terms of sample OKN SSC's, corresponding to each OKS speed. SSC samples and OKN frequency were subjected to additional statistical processing (cf. table 9). It was discovered that averages for standardized differences do not definitely differ from zero. Asymmetry dispersion decreases as stimulation speed increases. The distribution of OKN SSC calculated for each sample, combining all individual results obtained at the same stimulus speed regardless of direction (there were 78 ENG's in these samples for each stimulus speed) and at each of three stimulus speeds, exhibited statistically reliable positive asymmetry and positive excess. Since it has been shown that SSC distribution in nystagmic reactions of different origin (rotatory, caloric) is subject to lognormal law [129], comparison of logarithmic samples of OKN SSC revealed an OKN SSC difference for each of the three stimulus speeds which was statistically

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1 Problems related to the classification of nystagmometric characteristics and methods to calculate them are covered in chapter 3.

TABLE 8 /90

BASIC STATISTICAL INDICES FOR SSC SAMPLES AND FREQUENCY SAMPLES (39 ENG OKN'S) FOR THREE OKS SPEEDS

Nystagmometric Characteristic	OKS sec^{-1}	$\bar{x} \pm \sigma$	$\bar{y} \pm \sigma$	$\overline{(x-y)} \pm \sigma$	$r_{x, y}$	$R_{y/x}$	$B_{y/x}$	a	b	c
SSC, sec^{-1}	4	4.28±0.28	4.33±0.90	-0.055±1.318	-0.178	-0.196	5.147	1.546	0.502	1.280
	10	10.83±2.18	11.07±2.0	-0.192±1.477	0.753	0.692	3.540	0.487	-0.799	0.587
	20	20.52±1.68	20.59±2.19	-0.067±2.257	0.341	0.447	11.426	0.402	-0.21	0.236
Frequency (impulses per 20 sec)	4	5.26±2.12	5.72±3.13	-0.462±1.570	0.890	1.331	-1.175	1.070	-1.293	0.493
	10	14.59±6.25	14.51±5.83	0.077±3.557	0.829	0.773	3.235	0.082	-0.145	0.094
	20	20.79±8.37	22.41±8.93	0.385±5.923	0.768	0.829	7.737	0.035	-0.050	0.030

NOTE: $\bar{x} \pm \sigma$ -- arithmetic average and root-mean-square deviations for rightward OKN; $\bar{y} \pm \sigma$ -- same for leftward OKN; $(\bar{x-y}) \pm \sigma$ -- arithmetic average and root-mean-square deviation of the differences in characteristics of rightward and leftward OKN; $r_{x, y}$ - correlation coefficient; $R_{y/x}$ - regression coefficient; $B_{y/x}$ - free member of the regression equation; a, b, c - coefficients for second-type diagnostic formulas.

TABLE 9

OKN SSC AND FREQUENCY FOR THREE OKS SPEEDS

OKS Speed, sec^{-1}	Standardized Difference in OKN_r and OKN_l SSC, %				SSC of Initial Samples				SSC of Logarithmic				Frequency, sec^{-1}			
	x	σ	m	p	x	σ	m	CV,%	x	σ	m	CV,%	x	σ	m	CV, %
4	-0.6	±14.1	±2.3	+0.8	4.3	±0.9	±0.1	±21	1.44	±0.1	±0.02	±13	0.28	±0.18	±0.04	±28
10	-1.0	±6.3	±1.0	±0.4	10.9	±2.1	±0.2	±19	2.37	±0.18	±0.02	± 8	0.75	±0.25	±0.04	±34
20	-1.0	±5.0	±0.8	±0.9	20.6	±1.9	±0.2	± 9	3.02	±0.09	±0.01	± 3	1.14	±0.41	±0.06	±36

NOTE: p - probability of divergence from 0; CV - variation coefficient.

reliable in terms of Student's criterion (P less than 0.05). /91 This difference was not observed in terms of nystagmus frequency.

Materials introduced in Tables 8 and 9 show that, on the average, OKN's are symmetrical, their SSC's are close to stimulus speed (they can sometimes exceed it), and SSC variability decreases as stimulus speed increases. Individual asymmetry in a healthy child can be rather significant.[1]

1 See also the evaluation of OKN asymmetry based on mutual characteristic distribution (chapter 3).

Various forms of vestibular and, more rarely, optokinetic, nystagmus are now being studied in applied work. The diagnostic value of optokinetic tests in otorhinolarynology is much lower than that of vestibular. OKN is of primary interest to otoneurologists, who usually take into account the obvious damage to OKN's noted during visual observation. For example, it is believed that a pathology localized around the brain stem or near the cerebellum is indicated by OKN asymmetry only if it is combined with damage observed while testing the subject's gaze. If this test result is normal, then OKN asymmetry is considered to be a sign of hemispheric localization of the source of damage [406].

From the viewpoint generally accepted in vestibulologic practice, OKN disturbance lets us conclude basically that there is a pathology in the central nervous system, while we can only make assumptions regarding localization of the pathological source -- and then only infrequently. Thus we can state, first, that, at present, in contrast to vestibulometric tests which provide basic information in diagnostic studies of vestibular function, an optokinetic test is not very informative and is often only an ancillary technique. Second, it is obvious that both VN and OKN are regarded as particular independent reactions related only insofar as both reactions have the same activating mechanism: the eyeball with its musculature, motor nerves, and the nuclei of these nerves.

Another point of view, set forth previously in the form of a working hypothesis which has been to some extent confirmed in experiments, is considerably more attractive. These experiments showed that vestibular optokinetic nystagmus is actually a complex reaction quite different from vestibular nystagmus and from optokinetic nystagmus taken separately and that it is never the simple algebraic sum of these two types of nystagmus. Apparently, VOKN is important for an organism, i.e. as a certain entity into which VN and OKN are included as necessary components.

What sort of conditions would be considered ideal for normal /92
functioning of the system which creates VOKN? First, it is necessary that both subsystems (i.e. the systems which form VN and OKN) be sound. Without question, mechanisms which ensure interaction between the subsystems must also be in good working order. Finally, signals to each subsystem should not be contradictory, either in direction or intensity. In other words, only one of the existing vestibulometric tests satisfies the last requirement: rotation with positive acceleration with eyes open in light, i.e. under conditions in which eyes can fix on immobile objects surrounding the subject. All other situations can, to some degree, be considered conflicting. These include, for example, accelerated rotation in darkness, since under these conditions there are no signals in the optokinetic subsystem. Conflicts also include a test with purely optokinetic stimula-

tion produced by fixing the head in position (scarcity of vestibular signaling), as well as a test with negative angular acceleration in light (contradictory signals in subsystems), and many others.

In describing the so-called norm for VN or OKN using statistical methods, we must remember that, in and of themselves, these reactions occur under conditions not so much normal as conflicting. Having identified a pathology by comparing a particular observation with the norm, we must understand that deviations from the norm may be caused not only by a disturbance in the subject subsystem itself, but in the other subsystem connected to it, as well as in mechanisms coordinating the interaction of these subsystems. Consequently, having produced, for example, a nystagmic reaction whose characteristics differ from the mean statistical norm during an experimental vestibular test, we should not make too categorical a conclusion that the deviation is caused precisely by disturbances in the vestibular system itself. This conclusion becomes valid only if it is entirely certain that the optokinetic system is preserved. If it turns out that optokinetic reactions also deviate from the norm, then it would be quite natural to assume that the mechanisms which coordinate the subsystems or the mechanisms which ensure automatism of the whole VOKN system have been disturbed. This assumption in turn requires study of vestibulo-optokinetic reactions. In other words, obtaining a more complete understanding of the condition of the function under observation requires a test (or tests) which makes it possible to produce a VOKN in whose development both subsystems participate.

This task seems simple only at first glance. The difficulty lies in the fact that selecting the most appropriate test conditions requires appropriate analyses. The primary /93
obstacle in the first stages is that the considerations presented above are valid in terms of reactions produced in rabbits. However it is still necessary to determine to what extent these concepts are valid for human reactions.

Does Subcortical Optokinetic Nystagmus Exist in Man?

The need for development of a set of applied nystagmometric studies in which enough attention would be given not only to the parts of the a whole (i,.e. VN and OKN), but to the whole itself (VOKN), is obvious. The basis for this type of development is, of course, data obtained in a physiological experiment. However, the validity of this approach to solving the problem and its success greatly depends on the extent to which mechanisms by which nystagmic reactions form in man and in rabbits are similar -- more precisely -- on whether there are essential differences in these mechanisms. VN mechanisms in humans and rabbits are quite similar. In particular, the similarity amounts to the fact that, in both cases, nystagmus is a subcortical reaction, i.e. the cerebral cortex is not needed to produce

it. Otherwise it would be a matter of OKN, since, in and of itself, the physiological difference between human and rabbit visual systems prevents total mechanism similarity. Cortical sections of the cerebellum are not involved in formation of OKN in rabbits, but in contrast the role of the cortex in man is quite significant. In other words, OKN in a rabbit is subcortical[1], while in man the very possibility of producing subcortical OKN is problematic and is even generally denied by several authors. More will be said about this later.

Naturally, subcortical OKN mechanisms are of the greatest interest in comparing OKN and VN, and even more so since they define the mechanisms by which the two interact. This is because subcortical mechanisms are most likely to have the closest relationship with the vestibular system. Therefore, if humans were to exhibit subcortical OKN, it is precisely this reaction which would be of particular importance for applied nystagmometry. Subcortical OKN would be of interest in and of itself also as a component of a complex reaction -- VOKN. For this very reason, before we decide how VOKN research should be organized for applied purposes, it is important to determine whether subcortical OKN exists in man. If the answer is affirmative, this /94
reaction should be regarded primarily as a part of the whole.

Why has the question of the existence of subcortical OKN in man come up? The fact is that, in phylogenesis, oculomotor reactions become corticalized along with several primary functions (including visual). As a result, subcortical OKN mechanisms become even less important, being subordinated to cortical mechanisms. It is felt that cortical OKN is a form singularly inherent in man and that man has completely lost the subcortical optokinetic reaction.

This opinion has been expressed, for example, by Kornhuber, the author of several studies and a comprehensive review of the physiology and clinical picture of the vestibular system [405]. Proving his point of view, Konhuber refers to his own clinical observations, as well as to several facts taken from literature physiological in nature. His observations include for example the case of so-called cortical blindness caused by bilateral cessation of blood formation in the anterior medullar artery. The pathology was not associated with any symptoms indicating a disturbance in subcortical formations. The pupillary reflex was preserved in light. Nonetheless, a stable prolapse in OKN occurred. The following physiological facts were noted in this review. In rodents, OKN remains after bilateral extirpation of the visual cortex. Similar results have been obtained in experiments on cats, but in Rhesus monkeys OKN prolapse continues

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1 An experiment combining nystagmometric and electrophysiological research demonstrated the existence of subcortical and cortical components in OKN mechanisms in cats [472].

for several months after bilateral extirpation of the visual cortex.

These facts actually demonstrate a certain redistribution of the roles of subcortical formations and the cortex in phylogenesis: the cerebral cortex of rodents still plays little or no part in the formation of OKN, but the role of the cortex in apes is much greater. It is quite possible that this role is even more important in man.

On the one hand, these considerations indicate that the study of an OKN in whose formation the cortex would play a minimum role and which (in terms of its own mechanisms and level would be more like VN) would seem to promise certain advantages in diagnostics. On the other hand, we cannot ignore the commonly held opinion that a subcortical optokinetic reaction is entirely uncharacteristic of man. Hence it is clear why it is important to study whether subcortical OKN exists in man [122]. We will discuss a solution to this problem in more detail.

A working hypothesis for research can be formulated as follows. OKN in man can be produced with the subject paying active and insufficiently active attention to the optokinetic stimulus.

In practice during diagnostic study of OKN, the attempt is /95
usually made to mobilize the subject's attention. Special techniques have been proposed to do this (showing slides, et al.). Consequently, OKN asymmetry during such research should occur only in cases of gross disturbances to the central nervous system. Hence the first hypothesis: If the role of the cortex in organizing OKN is diminished (and with a pathology this role probably amounts to maximum possible correction of the disturbance), asymmetric OKN can be identified in more cases than is possible with ordinary research techniques.

As studies on children have shown, a rather stable OKN can be produced [134] even if the subject's active involvement is minimum. It is sufficient to increase screen dimensions and use an unmonotonous stimulus. In other words, OKN produced in children with the procedure described above, without any sort of instruction, can be considered more subcortical than cortical. Consequently, use of this stimulation procedure in studies on adults can be one factor promoting subcortical OKN. An additional technique which distracts the subject's attention can be used to reduce the cortex's participation in reaction formation.

There should be a qualitative difference between OKN's produced with active and distracted attention if these reactions are in fact caused by different mechanisms. Yet another hypothesis of this sort has been made. Pathological processes localized at various levels in the VOKN system should be associated with optokinetic reaction asymmetry and the nature of the

asymmetry may serve as a source of additional information on OKN mechanisms, permitting the differences in reactions to be defined.

These assumptions were confirmed in subsequent research in which electronystagmometric procedure was used to record the horizontal component in adult humans using cutaneous metal electrodes, an amplifier (time constant - 3 sec) and a fast-acting self-recorder. Twenty-second segments of ENG's were selected for evaluation, during which attention was paid to the form of nystagmic impulses and other features of the recording. If the forms on the recording were acutely disturbed, which hindered quantitative evaluation, evaluation was in some cases limited only to qualitative description.

Ten healthy subjects and 50 suffering from various forms of vestibular dysfunction, including those which are not associated with subjective complaints (480 ENG's), underwent examination.

The conditions of the experiments for studying optokinetic reactions were as follows. Before each recording, a subject was given one of the following instructions: 1) "Don't pay attention to the movement of the figure on the screen"; 2) "Watch the moving figure"; 3) "In your mind subtract 7 from 1000; then subtract 7 from the result and continue to subtract one 7 after another, looking at the screen." /96

For each stimulus movement speed, reactions were recorded six times, i.e. for each instruction OKN's were recorded with the stimulus moving to the left and to the right. The sequence in which the stimulus alternated and the pauses between stimulations were such that effects of adjustment and aftereffects were eliminated.

It was observed that OKN depends significantly on the instructions given to the subject. When instructed not to pay attention to the movement of the figure on the screen, most healthy subjects generally exhibited no optokinetic reaction. We know that this instruction should not necessarily cause such a pronounced inhibition of OKN [557]. These subjects were carefully questioned and it was discovered that they had fixed their gaze on any immobile point, i.e. they had actively curtailed eye movements.

In those cases when full OKN inhibition was impossible (even when the subjects actively tried to do so), the reaction was quite different than when they actively watched the moving figure: irregular nystagmic impulses in the form of a small group alternating with pauses, for which there was no nystagmic rhythm.

Analysis of ENG's recorded in healthy humans instructed not to pay attention to the movement of the figure showed, first,

that the instruction had a significant impact on the result; second, that OKN could be actively inhibited; and, third, that this particular instruction could not bring about a stable ON.

In all cases without exception, the instruction to watch the moving figure caused a definite optokinetic reaction. As a rule, the reaction differed somewhat in form from OKN nystagmograms usually obtained with an optokinetic drum with black and white stripes. Remember that the OKS was deliberately made not monotonous. Therefore even the OKN produced with this technique seemed somewhat atypical at first glance: impacts differed in amplitude and duration; i.e. frequency was not always regular. SSC was close to stimulus motion speed. Asymmetry, defined as the ratio of the difference in SSC's of optokinetic reactions in different directions to their sum, was usually no more than 5-7%.

The third instruction, intended to divert a subject's attention by solving a problem, in no case caused changes significant enough to be considered a clear inhibition of the reaction. Statistical processing and comparison of samples with the second and third instructions showed no significant differences in averages for SSC, frequency, and amplitude. /97

One might say that, given the traditional approach to comparing reactions, it was impossible to statistically observe certain differences between samples of optokinetic nystagmi obtained with the subject's attention focused and with it turned to solving a problem. Apparently, diverting attention to mentally solving an arithmetic problem in and of itself does not effect nystagmus formation in the norm enough to make the reactions differ from variations from the norm which occur with attention focused.

Note that literature indicates that nystagmic reactions are a function of instructions. Nystagmus caused by angular acceleration [277] is a function of the instructions given to a subject: if attention is concentrated on sensations of rotation, nystagmus is much weaker than if the subject is solving an arithmetic problem in his mind. The effect of various experimental conditions (including problem-solving) is also observed in studying a special form of eye movement -- fixational OKN occurring when the subject is instructed to focus his gaze at an immobile point on a contrasting moving background [39]. One might think that the effect of distracting or redirecting the subject's attention is not unequivocal and manifests itself differently in different forms of nystagmus.

Subsequent research on OKN's conducted on patients was intended to produce a picture of the primary variations in the asymmetry of optokinetic reactions which occur in a pathology and then, through analysis of these alternatives, to answer the question whether subcortical ON exists in man [122]. This

statement of the problem was based on the assumption that, if two forms of OKN actually exist in man, a pathology differing in terms of etiopathogenesis and localization may also be reflected differently in each form.

A group of patients formed as follows was examined. Patients sent for surdological treatment underwent vestibulometric examination if, on the basis of the condition of their auditory function, it was suspected that they had neuroma of the auditory nerve or another pathological process near the cerebellopontine angle. The primary general indicator on which the sample was based was unilateral disturbance of the auditory function [170]. Naturally, other symptoms were taken into account -- noise in the ears, gradual development of hypoacusis, a favorable otoscopic picture, etc. The patient sampling technique used could be considered somewhat random, since it permitted formation of a sample which was rather broad in terms of etiopathogenesis and level of injury. A sample of just this type was necessary to solve the problem -- to discover the basic variations of OKN asymmetry.

All patients first underwent BT, and the results were used to /98 calculate coefficients for labyrinth asymmetry (K_{LA}) and directional preponderance (K_{DP}). The group examined included only those who exhibited labyrinth dysfunction according to the results of BT evaluation using a diagnostic model (cf. chapter 4). Out of the total number of patients (50), 25 exhibited OKN asymmetry; the forms of asymmetry were quite varied. Reactions could be asymmetric only in terms of frequency or only in terms of SSC, but could involve both characteristics. Asymmetry involving disturbance of the structure of nystagmic impulses in one direction was also observed if nystagmus in the opposite direction was preserved. There were cases when asymmetry could be observed at one, two, or three stimulus angular velocities. This indicates the complexity of the problem of OKN asymmetry, which must be studied in detail in the future.

An attempt was made to systematize the material obtained in terms of only one indicator -- the presence of asymmetry -- regardless how this asymmetry was expressed: by a difference in quantitative characteristics, by a change in impulse form, or by combining these types of asymmetry. In other words, material obtained for each patient was evaluated to answer two questions: 1) Is there any asymmetry at all and what is the direction of the reaction which can be considered disturbed? 2) If asymmetry exists, is it observed in all experimental situations or only under one certain condition (e.g. only during active tracking of the stimulus with attention distracted)?

Comparisons were done in pairs. For example, a pair of ENG's recorded during stimulus movement from left to right and from right to left with identical angular velocity was compared

provided that, in both cases, the patient was solving an arithmetic problem in his mind.

When evaluations of the material were generalized (the results of which are given below), asymmetry was considered to be a fact even if it was observable only at one particular stimulus angular velocity.

Since the research resulted in rather conclusive confirmation of the existence of subcortical OKN in man, the term "subcortical optokinetic nystagmus" (OKN_{SC}) will be used below in presenting material to identify the reaction recorded during solution of an arithmetic problem, in contrast to the reaction produced during the subject's active involvement in the experiment, which will be called "cortical optokinetic nystagmus" (OKN_C).

Let us present the basic variations of OKN asymmetry and interpret the results. Several combinations (cf. figure 30) were discovered in which either OKN_C, OKN_{SC}, or both reactions could be considered asymmetric in the pairs of ENG's compared. /99

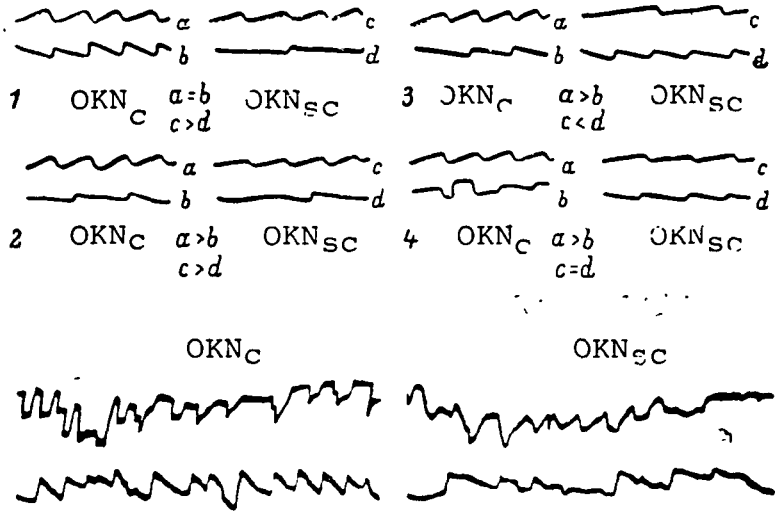

Figure 30. Variations in asymmetry (1-4) in two forms of OKN -- cortical (OKN_C -- a and b) and subcortical (OKN_{SC} -- c and d)

Below, an example of asymmetry related to variation 4 presented as fragments of ENG's obtained during examination of one patient.

1. OKN_C's symmetric, OKN_{SC}'s were asymmetric. 2. Both OKN_C's and OKN_{SC}'s were asymmetric. Deviation from the norm occurred in the same reaction direction. For example, if rightward OKN_C changed (weakened), rightward OKN_{SC} was also

less intense. 3. As in the previous case, both OKN_C's and OKN_{SC}'s were asymmetric. The difference is that reactions in different directions changed: OKN_C in one direction weakened when OKN_{SC} in the other direction weakened. 4. OKN_C's were asymmetric. OKN_{SC}'s were symmetric or their asymmetry was much less pronounced.

These variations in asymmetry are of great interest from the standpoint of the basic question whether subcortical OKN exists in man.

The first two types of asymmetry can be completely explained without hypothesizing that two forms of OKN exist. It is justifiable to imagine the mechanisms of these two variations of asymmetry to be approximately as follows. Let us suppose that two unidirectional reactions produced in the experiment, i.e. OKN_C and OKN_{SC}, do not differ substantially and are brought about by the same mechanisms, that the difference between them is purely quantitative. This difference may be due to the fact that, in the second reaction, through an artificial technique (solving an arithmetic problem), the cortex was somehow hindered in participating in controlling OKN, its role in correction was diminished, and, as a result, the reaction ceased to correspond to the stimulus. /100 If a certain sequence of links, a hierarchical chain, is involved in formation of OKN's in each direction, the highest and sole controlling link in the reaction is the cortical link, while development of OKN requires participation of all links. Now let us imagine that some sort of disturbance has occurred in one of the lower links. The degree to which this disturbance is externally manifest, i.e. the change in OKN, should depend on the extent to which the higher link can correct the disturbance. If the higher link is in satisfactory condition and the level of disturbance in the lower link is minor, total correction is possible and OKN_C in both directions will be identical, i.e. symmetry will not be violated. If use of an artificial technique diminishes the role of the cortical link, total correction is difficult. The disturbance in the lower link then becomes obvious and is manifested by OKN_{SC} asymmetry. A greater disturbance in the lower link can make total correction impossible. In this case not only OKN_{SC}'s, but also OKN_C's are asymmetric, i.e. the second variation on asymmetry occurs, in which the sign of asymmetry in both reactions is the same.

The second variation of asymmetry can occur when a disturbance occurs in the cortical link itself, which not only loses its capacity for correction, but serves as a source of asymmetry. Thus there is no need to assume the existence of two different types of optokinetic reaction (OKN_C and OKN_{SC}) to more or less plausibly explain the first two variations on asymmetry, since the second reaction (i.e. OKN_{SC}) is simply a somewhat weakened version of the first.

However, observation of the third and, especially, the fourth variations requires that we reject this simple plan and assume the existence of two OKN mechanisms -- cortical and subcortical.

The third variation observed is intersecting asymmetry: OKN_C is weakened in reactions in one direction, while OKN_{SC} is weakened in reactions in the other; if, for example, a disturbance in rightward OKN_C is accompanied by a disturbance in leftward OKN_{SC}. Approaching this formally, i.e. assuming that rightward and leftward reactions are formed independently, we can consider reactions in each direction separately. For example, the genesis of a disturbance in leftward OKN_{SC} if leftward OKN_C is preserved can be represented just as the origin of the first variation on asymmetry presented above is, i.e. inadequate cortical correction. The assumptions made earlier are plainly inadequate to explain the origin of simultaneous disturbances occurring in rightward reactions. According /101
to the initial pattern, disturbances in the upper link, if it is actually the only controlling link, must necessarily be seen in a reaction both when this link is involved in actively organizing OKN (i.e. in OKN_C) and when it is involved passively (i.e. in OKN_{SC}). Since rightward OKN_{SC} did not suffer, regardless of an obvious disturbance in rightward OKN_C (i.e. an indication of pathology in the higher link), we have to assume that OKN is controlled not only at the higher, but also at the lower level. In other words, we must assume that there is an "independent" (we will use this word in quotation marks for the time being) mechanism of subcortical optokinetic nystagmus.

In general, the third variation on asymmetry is quite complex, since we must assume a localized pathological center with which this center can disturb optokinetic reactions in one direction at one level and reactions in the opposite direction on another. It is quite probable that intersecting effects and relationships, about which there is still not enough data, are present. However, regardless of these complexities, the very fact that the third variation on asymmetry exists is important in the sense that it forces us to assume the existence of optokinetic reaction control not just on the cortical, but on the subcortical level as well.

The last variation on asymmetry, i.e. the fourth, is of greatest interest. In this variation, reactions in one direction are preserved, while, in reactions in the the other direction, only OKN_C's are disturbed. Here the relative autonomy of the OKN_{SC} mechanism is seen in its pure form.

The fourth variation also encompasses cases when OKN_{SC}'s are not completely symmetric, but the asymmetry of these reactions is expressed to a much lesser extent than OKN_C asymmetry.

Figure 30 demonstrates this example. It is quite obvious that OKN_{SC}'s are not entirely identical. Nonetheless, the "injured" OKN_{SC} consists of typical two-phase nystagmic impacts, with SC's directed to one side. In contrast to subcortical OKN's, cortical OKN's are acutely asymmetric. In leftward OKN_C there are generally no typical nystagmic impulses. Instead there are jumps unordered in their direction. OKN's in this case were studied twice over an interval of several days, and the results were identical.

The statement of the problem and the procedure used to select patients in this case prevented any sort of statistical evaluation, including that of frequency. Nonetheless, we might note that the fourth variation on asymmetry is not a rare exception, since it applied to four patients. Figure 31 gives some examples of this asymmetry.

/102

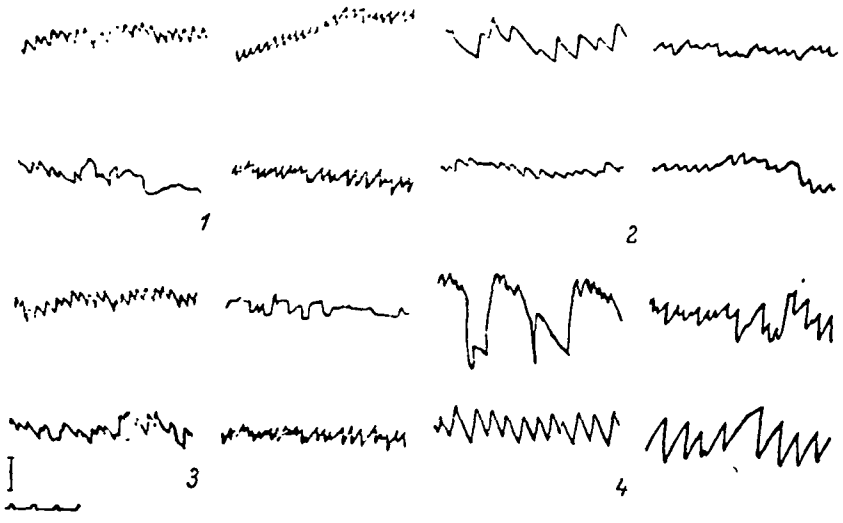

Figure 31. Variations on OKN asymmetry.

Each example (1-4) is represented by four ENG's: a pair of OKN_C's opposite in direction (upper ENG's) and a pair of OKN_{SC}'s (lower) at OKS $20^\circ \cdot sec^{-1}$.
1 -- OKN_{SC} asymmetry; 2 -- OKN_C symmetry;
3 and 4 -- examples of intersecting asymmetry.
Calibration: 20°, 1 sec.

Study of the primary variations on OKN asymmetry revealed the basic possibility of separate "failures" in OKN_C's and OKN_{SC}'s, especially the possibility of significant disturbance of the first while the second is preserved. This fact indicates that, in addition to the mechanism of cortical OKN, there is, in fact, another mechanism, subcortical OKN. Under normal circumstances, the cortical mechanism is predominant,

but in others (e.g. with attention distracted), the subcortical mechanism may function somewhat autonomously of the cortical.

Since the technique used in this article was required to discover these facts, the procedure can be considered adequate for studying two forms of optokinetic reaction -- cortical and subcortical. Names which initially were assigned conditionally to the optokinetic reactions (i.e. OKN_C and OKN_{SC}) can apparently be used with full confidence, since they reflect the essence of these reactions. Here we must emphasize that classification of the reactions as cortical and subcortical forms cannot be considered analogous to division into "foveal" and "retinal" OKN, since the latter are produced with different optokinetic stimuli. In the experiments described above, the stimulus for producing both OKN_C and OKN_{SC} was the same. Approaching this formally, we can state that both nystagmi studied were retinal in terms of the method of stimulation.

The practical conclusion is that OKN research for applied purposes cannot be limited to study of nystagmus which occurs /103
while the subject is actively tracking a moving stimulus, since, with this approach, some asymmetry may remain undetected. The resulting opinion on the comparative rarity of OKN asymmetry during vestibular dysfunction has been, as one might imagine, a result primarily of the fact that it is the subcortical OKN which is affected, while research traditionally focuses on cortical OKN. Finally, there is no longer any doubt that development of a nystagmometric test to study VOKN requires conditions optimum for the activity of subcortical OKN mechanisms. The following conclusions result from this research.

1. Man does not lose subcortical OKN mechanisms during phylogenesis, although cortical mechanisms are quite dominant. 2. Detecting subcortical OKN requires use of additional techniques. One technique can be distracting the subject's attention to solving an arithmetic problem in his mind. 3. Diagnostic studies can entirely eliminate OKN asymmetry only if both forms of the reaction, i.e. OKN_C and OKN_{SC}, are symmetric.

Experimental Research on the Possibility of OKN Asymmetry in Man due to the Influence of Changes in the Vestibular System

In diagnostic practice, the concept that OKN asymmetry occurs only as a result of injuries to the central nervous system is considered almost axiomatic. Besides, it is apparently impossible to deny that even peripheral vestibular dysfunction may cause OKN asymmetry. This has been confirmed by an article [11], which indicates that OKN can change during cochlear neuritis. From the theoretical standpoint, this is a question regarding the mechanisms by which VOKN forms during a conflict created by asymmetric conditions in the primary vesti-

bular afferents. From the practical standpoint, it is a matter of the possibility that OKN asymmetry results from changes in the vestibular system and of the diagnostic importance of this asymmetry for applied vestibulology.

Several conditions had to be satisfied if this problem was to be solved. First, OKN had to depend as little as possible on cortical control. It is precisely for this reason that the research was done on children [139]. Second, the model for vestibular dysfunction had to be those changes which, in and of themselves, could cause nystagmus, i.e. a super-threshold vestibular stimulus was required so that its effect would be clearly noticeable. Third, it was necesssary to select vestibular and optokinetic stimuli so that the VN and OKN they caused independently would be similar in intensity, since it would thus be possible to obtain a qualitative understanding of the weighted relationships of the two subsystems (vestibular and optokinetic) /104

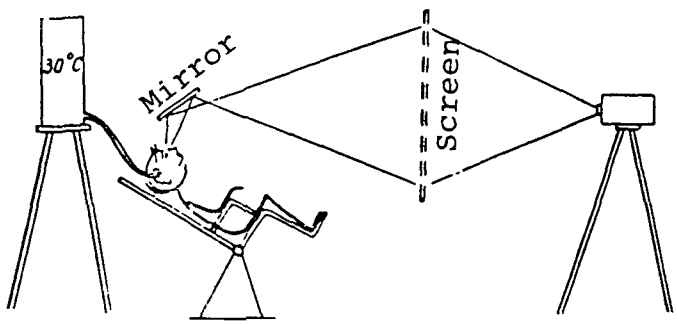

Figure 32. Set-up for simultaneous caloric and optokinetic stimulation.

OKS is projected on a matte screen by a projector through whose film track film glued into a loop is projected at a constant speed. The subject is placed in a position optimum for caloric testing and sees the image of the moving OKS on the back of the screen by means of a mirror.

in a single vestibulo-optokinetic system, as well as to be sure how valid is the conclusion, made during a physiological experiment, that the relationships differ from the simple algebraic sum of the reactions when applied to man. Fourth and finally, it was necessary to change vestibular afferentation only on one side, i.e. to simplify experiment conditions and the corresponding results as much as possible.

Thirty children aged 4 to 7 were examined. The subjects were given no instructions whatsoever. The vestibular stimulus was irrigation of the right exterior acoustic meatus (30°C, 100

ml). The study was conducted on a stand which allowed a subject sitting in a chair to be tilted backward in the sagittal plane as required for the test. The stand was equipped with a mirror so that a subject could see the optokinetic screen located in the vertical plane (cf. figure 32). All recordings were made with the subject in the same position. ENG's were recorded under the following conditions: 1) a cool test on the right ear -- horizontal VN to the left (1 ENG); 2) OKN to the right and left at OKS $20^{\circ}\cdot sec^{-1}$ and at OKS $10^{\circ}\cdot sec^{-1}$ (2 ENG's); 3) cool tests on the right during OKN to the right and OKN to the left, which produced OKN in two directions at two OKS speeds (4 ENG's). Nine reactions, which were analyzed quantitatively, were recorded for each subject.

The same abbreviations as in the previous study [75] were used to identify the different forms of nystagmus, i.e. VOKNC and VOKNN, depending on whether the directions of the OKN which provided the background and the potential VN coincided or not. SSC's over 10-sec segments were used to evaluate intensity. A segment of a stable reaction was taken to measure OKN; an extreme section (i.e. the maximum in terms of SSC for VOKNC and the minimum for VOKNN) was taken to measure VOKN. All children exhibited otiatric anamnesis, but their otoscopic condition, acoumetric data, and neurological status did not justify suspecting ear or eye pathology. /105

It has been established that OKN caused by OKS movement changes if a monaural cool vestibular test is made during continuous optokinetic stimulation. These changes are qualitatively identical in different subjects. They amount to intensification or weakening of the nystagmus depending on whether background OKN and potential VN match in direction. These changes in nystagmic intensity are henceforth called modulations: OKN -- modulatable nystagmus; VN during isolated cool stimulation (i.e. caloric leftward nystagmus -- modulating nystagmus; VOKNC and VOKNN -- modulated nystagmi). In all cases, the index "r" or "l" in this series of studies indicates nystagmus direction. For example, CN_l means leftward caloric nystagmus, OKN_r -- rightward optokinetic nystagmus, etc.

Let us consider first the results of modulating OKN at an OKS of $20^{\circ}\cdot sec^{-1}$ (cf. table 10, A). The mean arithmetic $VOKNC_l$ SSC is certainly greater than the SSC of the OKN_l to be modulated. The difference between $VOKNN_r$ and the nystagmus to be modulated is statistically uncertain. However, the difference between reactions is clear, and the existence of statistically certain (P less than 0.05) inhibitions in terms of sign has been demonstrated. Given a modulating action, reactions become asymmetric. If initial OKN's can be considered symmetric, then the average of the absolute differences between $VOKNC_l$ and $VOKNN_r$ will be $12^{\circ}\cdot sec^{-1}$, while that of the relative differences will be 30%. At OKS $10^{\circ}\cdot sec^{-1}$ (cf. table 10 B), the result was qualitatively similar, although the

certainty of the modulating effect was confirmed only by the signs. Absolute asymmetry averaged 8.5°·sec^{-1}; relative -- 37.8%. At both OKS's the inhibiting effect was less significant than the exciting effect.

There is nothing surprising in the fact that additional vestibular stimulus has a modulating effect on OKN, as facts above have already indicated. However, it is important, first, that this effect was produced in terms of subcortical OKN and that vestibular afferentation was subject to change only on one side. Second, the fact that the effectiveness of a particular modulating action differs with different background reactions is new, and it is clearly significant for the small OKS which defines background activity. If both subsystems in the experiment had been completely equitable, then it would have been natural to obtain the algebraic sum of the two forms of nystagmus; but this was not the case. Moreover, when VN and OKN acted as competitors, it turned out that the retarding /106

TABLE 10
THE EFFECT OF MODULATION AT (A) OKS 20°·SEC^{-1} AND (B) 10°·SEC^{-1}: STATISTICAL INDICES OF THE SSC SAMPLES FOR MODULATING (CN_l), MODULATABLE (OKN_r and OKN_l), AND MODULATED ($VOKNC_l$ AND $VOKNN_r$) NYSTAGMIC REACTIONS

Sample	A			
	$\bar{x}$	m	σ	CV, %
1. CNl	12.67	±1.90	±0.68	±15.032
2. OKNl (a)	19.82	±1.02	±0.37	± 5.15
3. OKNr (b)	19.68	±1.43	±0.51	± 7.29
4. VOKNCl (c)	26.46	±2.16	±0.77	± 8.15
5. VOKNNr (d)	14.48	±1.53	±0.55	±10.53
6. a-b	0.15	±1.26	±0.45	-
7. (a-b)/(a+b)	0.004	±0.032	±0.012	-
8. b-d	5.20	±2.15	±0.77	±41.32
9. c-a	6.63	±2.33	±0.84	±35.16
10. c-d	12.00	±3.15	±1.12	-
11. (c-d)/c+d)	0.292	±0.071	±0.025	-

Table 10 (cont)

Sample	B			
	$\bar{x}$	m	σ	CV, %
1. CN1	12.67	±1.90	±0.68	±15.03
2. OKN1 (a)	10.36	±1.19	±0.43	±11.45
3. OKNr (b)	10.28	±1.43	±0.51	±13.91
4. VOKNC1 (c)	15.54	±2.09	±0.75	±13.49
5. VOKNNr (d)	6.97	±1.07	±0.48	±15.42
6. a-b	0.08	±1.57	±0.56	-
7. (a-b)/(a+b)	0.006	±0.078	±0.028	-
8. b-d	3.32	±1.54	±0.55	+46.35
9. c-a	5.15	±2.63	±0.94	±51.07
10. c-d	8.54	±2.51	±0.90	-
11. (c-d)/c+d)	0.378	±0.091	±0.033	-

effect was less pronounced than if background OKN was smaller. Average intensity of caloric nystagmus ($12^{\circ}\cdot sec^{-1}$) not only was not less than, but actually exceeded the average intensity of the OKN to be modulated somewhat ($10^{\circ}\cdot sec^{-1}$). Nonetheless, average intensity of modulated (inhibited) OKN turned out to be unexpectedly high (about $7^{\circ}\cdot sec^{-1}$). Finally, we must note another interesting fact: at OKS $20^{\circ}\cdot sec^{-1}$, total modulation depth (i.e. the difference between $VOKNC_l$ and $VOKNN_r$) averaged $12^{\circ}\cdot sec^{-1}$, i.e. it almost equaled the intensity of the modulating VN ($12.7\cdot sec^{-1}$). Naturally, this may be simply an accidental correspondence. Therefore, it /107 is necessary to determine what kind of relationships exist within the limits of individual results. Study of correlations is required to answer this question, as well as several others which inevitably arise when averaged calculations are used. Tables 11 and 12 present the results. As in the previous case, it is convenient to start with experiments at $20^{\circ}\cdot sec^{-1}$. The most significant facts are given below.

1. Initial OKN's are interrelated, which is quite natural. However the correlation is not strong (cf. table 11).

2. The intensity of the modulating nystagmus is apparently not decisive in terms of the depth of the modulating effect (both inhibiting and intensifying).

TABLE 11
SSC CORRELATION FOR ENG SAMPLES FOR EACH OF TWO OKS's: (A) 20 AND (B) 10 $^{\circ}\cdot SEC^{-1}$

ENG Samples Compared		Correlation Coefficient	
		A	B
OKNr	OKN1	0.514	0.296
VOKNC1	VOKNNr	-0.437	-0.173
OKNr	CN1	-0.129	0.297
OKN1	CN1	-0.342	0.106
VOKNC1	CN1	-0.159	0.406
VOKNNr	CN1	0.166	0.148
CN1	VOKNC1-VOKNNr	0.190	-0.275
OKNr-VOKNNr	CN1	-0.204	0.173
VOKNC1-OKN1	CN1	0.003	0.275
OKNr-VOKNNr	OKNr	0.705	-0.117
VOKNC1-OKN1	OKN1	-0.386	-0.189

TABLE 12
CORRELATION BETWEEN IDENTICAL SAMPLES, ONE OF WHICH WAS OBTAINED AT (A) OKS= $20^{\circ}\cdot SEC^{-1}$, THE OTHER AT (B) OKS = $10^{\circ}\cdot SEC^{-1}$

Samples Compared		Correlation Coefficient
A	B	
OKNr	OKNr	-0.159
OKN1	OKN1	-0.064
VOKNNr	VOKNNr	0.082
VOKNC1	VOKNC1	-0.245
OKNr-VOKNNR	OKNr-VOKNNr	-0.079
VOKNC1-OKN1	VOKNC1-OKN1	-0.197
VOKNC1-VOKNNr / VOKNC1+VOKNNr	VOKNC1-VOKNNr / VOKNC1+VOKNNr	-0.229

3. Modulation depth is much more related to the initial nystagmus to be modulated: the more intense the OKN to be modulated, the greater the inhibiting modulation. However, there is a negative correlation between intensifying modulation and the intensity of the nystagmus to be modulated. /108

4. A negative relationship also exists between modulated reactions: the smaller the VOKNN SSC, the larger the VOKNC SSC and vice versa.

5. The modulating nystagmus (CN_1) correlates weakly only with the OKN_1 to be modulated, i.e. nystagmus in the same

direction; it is apparently not related either with OKN_r or with VOKNC or VOKNN.

These are the results of correlation analysis, provided that a sufficiently strong OKS (i.e. $20^{\circ}\cdot sec^{-1}$) is used. With a smaller OKS ($10^{\circ}\cdot sec^{-1}$) the results can generally be considered similar. Comparing results of two stimuli revealed two exceptions to this similarity. The first involves the relationship between modulating nystagmus and VOKNC, which has been observed at $10^{\circ}\cdot sec^{-1}$. The greater the modulating nystagmus's SSC, the greater the VOKNC SSC. The second exception applies to the relationship between the nystagmus to be modulated and the magnitude of the inhibiting effect: in contrast to what happened at $20^{\circ}\cdot sec^{-1}$, the magnitude of the inhibiting effect at $10^{\circ}\cdot sec^{-1}$ was clearly unrelated to initial OKN.

Table 12 gives the results of a search for the statistical relationships of like reactions, as well as between like modulating effects which were produced at two different OKS's. In contrast to the previous task, where samples of identical OKS intensity were compared, the other side of the question was studied: to what extent can the observed quantitative changes due to modulation be considered similar at two different OKS'S? The result was surprising: clearly, these relationships are problematic and, possibly, do not exist at all. It was not possible to find definitive evidence that there is a correlation, even where it would be completely natural. For example, there is no connection between initial OKN's if they have been obtained with different stimuli. No connections have been observed between like modulated nystagmi, between modulation depths, or between the magnitudes of relative asymmetry. In other words the impression is created that the difference between OKN's caused by two different stimuli (20° and $10^{\circ}\cdot\cdot sec^{-1}$) is much more important than the quite natural quantitative difference in intensities. This problem apparently deserves more serious study and categorical conclusions cannot yet be made, since only two stimulus intensities have been used. However, at this stage, we can say that an OKS of $20^{\circ}\cdot sec^{-1}$ is preferable to one of $10^{\circ}\cdot sec^{-1}$ in applied research.

The fact expressed in table 11 that there is no correlation between $VOKNC_1$ and CN_1 intensities at OKS = $20^{\circ}\cdot sec^{-1}$ is interesting. It would seem to indicate that the coincidence /109 of average total modulation depths (c-d = $12.00^{\circ}\cdot sec^{-1}$, cf. table 10) and average CN intensity ($12.67^{\circ}\cdot sec^{-1}$, cf. same table) is accidental, i.e. that modulation depth is not a function of the intensity of the modulating nystagmus. However, we apparently cannot deny this relationship entirely, since a connection has been observed at OKS = $10^{\circ}\cdot sec^{-1}$: the coefficient for the correlation between $VOKNC_1$ and CN_1 equals 0.406 (cf. table 11). Keep in mind also that this was noted as

one of the exceptions. The second exception can be compared with this, namely the inhibiting effect (b-d) which does not correlate with OKN_r at $10^{\circ}\cdot sec^{-1}$, although the correlation is obvious at $20^{\circ}\cdot sec^{-1}$. Similarly, the exciting effect is more completely manifest when the reaction to be modulated is less intense. In contrast, the inhibiting effect is less intense on a background of OKN. In other words, we can assume that initial conditions, i.e. the background activity of the vestibulo-optokinetic system, do make a difference in the modulating effect. If activity is rather high, then it is difficult to increase it further by additional actions; and if it is low, decreasing it is difficult.

Since background activity of the vestibulo-optokinetic system in these experiments depended on the activity of the optokinetic subsystem, one of the conclusions and hypotheses we might make for further research in this direction could be that, in conflict conditions created by unilateral reduction in labyrinth afferentation (cool test), the optokinetic subsystem is more important than the vestibular.[1] A second conclusion is that, during unilateral reduction in labyrinth afferentation, there is no algebraic summation of nystagmi.[2] Despite the high intensity of the cool nystagmus, which could be produced with isolated vestibular stimulation, potential VN, which somehow interacts with OKN, does not produce as pronounced an inhibiting or exciting effect as we might expect. In fact, the inhibiting effect is about half. Under the conditions in which the conflict model was studied, the residual activity of the vestibulo-optokinetic system (i.e. $VOKNN_r$ SSC) was not a function of potential VN intensity (if the latter was commensurate with OKN), but, at the same time, this activity is clearly related to optokinetic stimulation intensity: at a stimulus of $20^{\circ}\cdot\cdot sec^{-1}$ it was twice that at $10^{\circ}\cdot sec^{-1}$. This may be a third conclusion.

On the basis of comparing the first and third conclusions, /110 we can assume that OKN intensity results only partially from the activity of multimodal neurons in the vestibular nuclear system, but that there is still a certain activity in the vestibulo-optokinetic systems which is sufficiently independent of the vestibular subsystems and that this activity is responsible for the level of residual activity. Further research should show how valid this hypothesis is.

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1 The dominant role of the visual system in optico-vestibular interaction can be evaluated in terms of results obtained during research on humans using sinusoidal rotation [419].

2 The opinion that the interaction occurs in terms of a simple algebraic summation is often found in literature (cf. for example [578]), but no definite evidence has been produced.

We can state that a certain amount of asymmetry in OKN's observed in the clinic is also due to similar causes, i.e. asymmetry of vestibular afferentation. The next task in work in this area is to find a way to differentiate these types of OKN asymmetry. Judging from certain literature (cf. for example [377]), solving this problem may require additional techniques, since ordinary OKN research intended only to assess reaction symmetry may be inadequate. It is possible that this comparison of modulated OKN_{SC}'s which differ in direction may be suitable for such a purpose.

To summarize this chapter, we can note that the continuity between experimental-physiological research conducted on rabbits and studies on humans under conditions close to clinical have had a positive result. Most important theoretically is confirmation of the fundamental hypothesis that subsystems which form vestibular and optokinetic nystagmus interact quite closely and that this interaction is substantially more complex in terms of regularities than simple algebraic summation of two oculomotor reactions. It has been possible to discover new facts pertaining to quantitative aspects of the relationship. In particular, it has been observed that, when the subsystems are in conflict due to unilateral change in vestibular afferentation, the optokinetic subsystem plays a leading role in formation of vestibulo-optokinetic nystagmus. This can be judged, albeit not completely, by the fact that it is impossible to fully inihibit OKN, even when potential VN is more intense. It is quite probable that the widely held opinion that OKN asymmetry arises only as a result of a localized pathological process at a rather high level may be due to similar peculiarities. As experiments on humans have shown, conditions can be created during which asymmetry resulting from artificially created peripheral vestibular dysfunction becomes clear and, even with statistical certainty, different from the variations typical of the norm. The most important of these conditions include careful nystagmometric evaluation of OKN and attention to the subcortical form of the latter.

Chapter 3. Nystagmometric Approaches To Increasing the Information Value of Vestibular Tests /111

Problems Systematizing Nystagmometric Characteristics

Successful identification of a pathology by comparison with the norm greatly depends on how completely the subject reaction is described and especially on the assumptions underlying the description of the norm. As regards vestibular nystagmus, these assumptions cannot be considered developed [19, 228]. Complete description requires a set of indicators (quantitative characteristics) which adequately reflect the most important features of the nystagmus. The search for these indicators, begun along with development of the first nystagmometric procedures, continues to this day [172, 173, 359, 364, 453, 524]. Computer technology and special nystagmometric devices have promoted progress in this area [337, 364, 444, 489-491]. Because of the abundance of nystagmometric characteristics which can be found in literature devoted to study of the condition of the vestibular apparatus, there is a pressing need to order and systematize them. We must reach the point where this literature will provide exhaustive indications of the kind of nystagmic characteristic and just how it was measured. For example, a reference such as "frequency was studied" must be considered plainly inadequate. First, frequency varies over the course of the reaction. The term "frequency" can be applied to an individual nystagmic impulse, to a group of impulses over a given time, to impulses in the area where nystagmus culminates, etc. These characteristics have different meanings. Second, vestibulometric study restricted to just one frequency measurement is often not enough of an assignment.

One attempt to systematize nystagmometric characteristics [148] was made during analysis of ENG's recorded in virtually healthy people subjected to rotation tests. Trapezoidal rotation programs at various angular accelerations and stimulus durations were used. Nystagmus was recorded with eyes closed. The task amounted to evaluating nystagmograms by various means, comparing the results obtained by different evaluation techniques, and defining the nature of the change in parameters over the course of the reaction, as well as their relationship with stimulus intensity. The study of caloric nystagmic reactions /112 in healthy people, as well as development of new diagnostic nystagmometry techniques, is a continuation of research in this direction [128, 129, 423].

For practical purposes (especially to prevent misinterpretation), it is convenient to divide all nystagmometric characteristics into elementary, dynamic, and total. Each elementary characteristic (i.e. one which describes a particular feature of an individual nystagmic impulse) can be used, depending on the purpose of the research, either to construct a dynamic characteristic or to calculate the total characteristic.

Dynamic characteristics (DC) are those which reflect the dynamics -- changes occurring in a certain elementary characteristic -- over the course of the reaction.[1] DC's can be indirectly used to evaluate cupuloendolymphatic dynamics and mechanisms by which nystagmus is controlled. Dynamic characteristics are also suitable for identifying certain general principles inherent in a set of reactions obtained under identical experimental conditions. In this case, DC can be presented as the result of averaging several individual dynamic characteristics. Averaging is done for consecutive equal segments of the time scale. DC's can be represented in the form of a table or graph. The X-axis of the graph which thoroughly describes a DC represents time; the Y-axis -- a particular elementary characteristic in absolute or relative units. The forms in which DC's are presented may be quite diverse. In the simplest case, each nystagmic impulse is represented on the graph by a point whose coordinates are time (e.g. the moment the impulse begins) and the absolute value of the characteristic measured (e.g. SSC, $^{\circ}\cdot sec^{-1}$. The time axis may be broken down into more or less large segments (e.g. 5 or 10 sec) and the results of measuring impulses within each segment may be averaged. This technique is especially convenient for identifying general principles in terms of the ENG sample. Rating the characteristics at each point on the graph (e.g. according to an individual maximum) makes it possible to produce a common scale for samples, regardless of individual variations.

Let us present certain examples. Figure 33 shows the dynamics of slow component amplitude during positive acceleration (the result of averaging over an ENG sample). Each individual result was rated in terms of the maximum. The instability of the characteristics and the presence of a local maximum are quite evident. Figures 34 and 35 demonstrate DC's with a different meaning: they present a total over time -- the increment in the number of impulses over time. In the first case (cf. figure 34), average nystagmus frequency is a function of stimulus: it increases as angular acceleration increases. In the second (cf. figure 35) the reaction is different and frequency remains unchanged. Figure 36 gives an example of DC's called vestibulograms, used in diagnostic research [462, 464]. /113

Note that pathological stimulation of the right labyrinth occurred in this example [48]. This way of representing DC is convenient for comparing nystagmi caused by stimuli with different signs (right- and leftward rotation) or identical stimuli applied to different labyrinths (e.g. a cool test from right to

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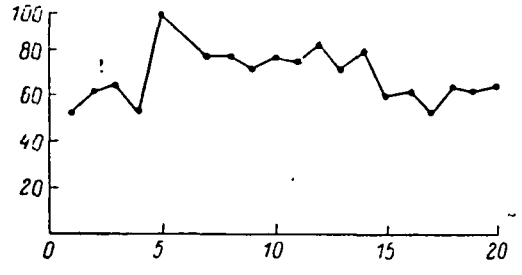
1 The term "dynamic characteristic" was later used also to designate the curve representing nystagmic reactions as a function of discretely manifested stimuli of different intensity [177], i.e. this term was imbued with a different content.

left). DC's are also convenient for identifying the relationship between different nystagmus parameters. DC's are quite important for studying adaptation mechanisms and other processes when it is important to account for changes in characteristics over time [42, 115, 116].



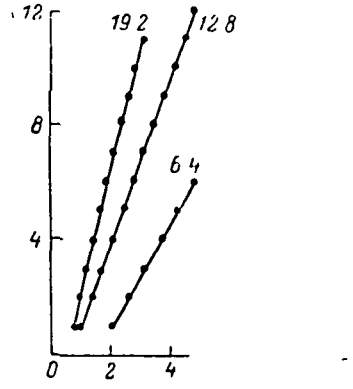


Figure 33. Dynamic characteristic of nystagmus -- VVN ASC (from [148]).

X-axis -- time from the onset of the effect of positive angular acceleration ($6.4^{\circ}\cdot sec^{-1}$ over 9.4 sec.), sec. Y-axis -- ASC, % of the value at the fifth second (the result of averaging a sampling of 21 ENG's).

Figure 34. Dynamic characteristic of nystagmus -- the increment in the number of nystagmic impulses over time (from [148]).

The result of evaluating three ENG's from one subject, recorded at different rates of positive angular acceleration ($^{\circ}\cdot sec^{-1}$), identifed for each curve. X-axis -- time when the stimulus took effect, sec. Y-axis -- number of impulses. Average nystagmus frequency reflected by the steepness of the curve's slope is clearly different.

DC's were used to study the relationship between nystagmus and stimulus force and additional otolithic organ stimulation, as well as to study the interaction between vestibular and optokinetic nystagmi and several other problems [50-52, 75, 78, 79, 107, 112-115, 118, 148, 187, 422].

In contrast to DC's, total characteristics (TC's) provide a somewhat limited understanding of the nystagmic reaction, since they are expressed by only one number. They are calculated as the average over the entire reaction or as the average over a given time. For example, SSC for the so-called reaction culmination section is often calculated to express nystagmus /114

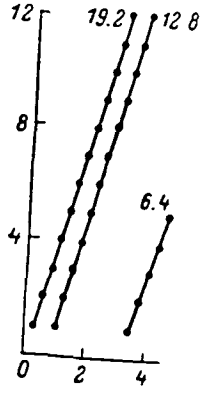


Figure 35. Dynamic characteristic of nystagmus -- increment in the number of nystagmic impulses over time (from [148]).

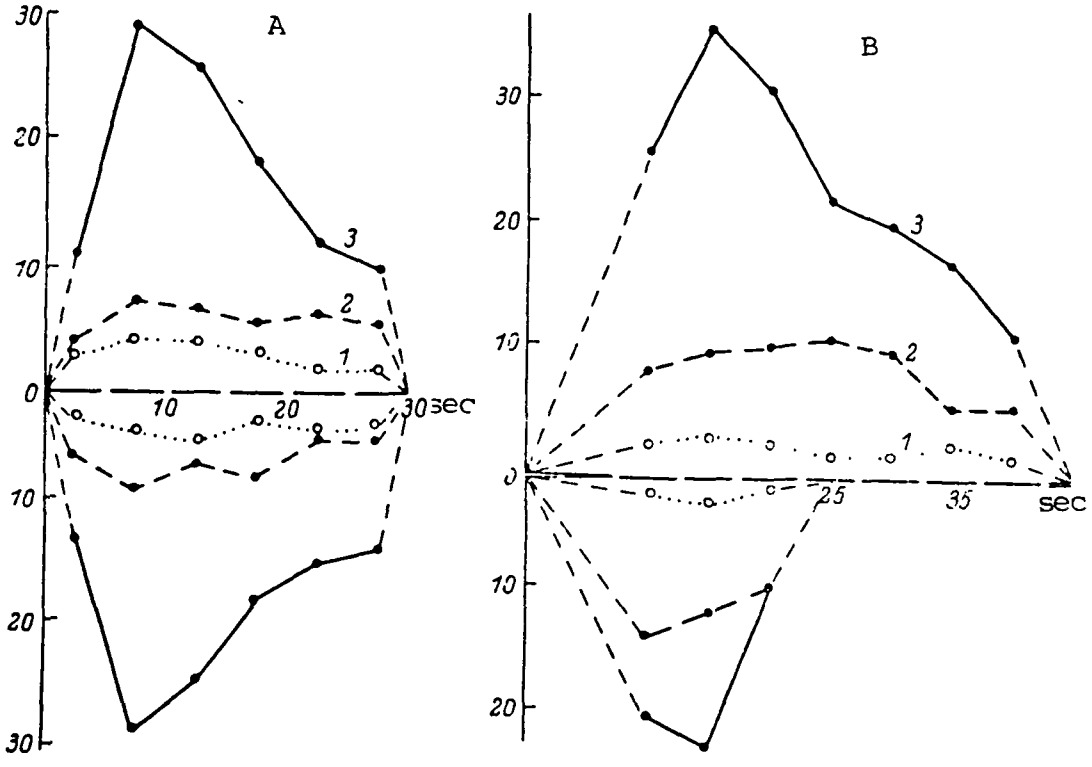
The result of evaluating three ENG's from one subject obtained under the same conditions as in figure 34. The labels are identical. The steepness in the slope of curves for different stimuli is identical.

intensity and, sometimes, maximum SSC in the literal sense is used regardless of how strictly local, i.e. found in just one impulse, it might be. TC's are used much more often in nystagmometric research since they are simpler to obtain than DC's and they are convenient when statistical evaluation techniques are to be used.

TC's have been used to solve several problems: to review the correlation between parameters, to construct a diagnostic model, to study the effect of sound on nystagmus etc. [116, 120, 136-138]. TC's are especially important in diagnostic research, since they are quite convenient in comparing reactions. These characteristics were so named because as the product of averaging, they can provide a generalized evaluation of a reaction [148].

Several interesting regularities involving DSC and its dynamics as a function of angular acceleration and the duration of its action have been observed during research on rotatory reactions using these approaches. An observation made previously during study of rabbit nystagmus [102, 112] concerning a possible mechanism for stabilizing frequency by redistributing SC and FC within the nystagmic impulse was confirmed during research on human nystagmus. It was shown that DSC dynamics depend more on this redistribution than on changes in nystagmus rhythm (or, correspondingly, the duration of the entire nystagmic impulse). It was established that, in healthy humans, the difference in the areas under the curves on vestibulograms for right- and leftward nystagmus may reach 30%. Certain relationships between various parameters within the limits of the reaction and the relationship of several characteristics to stimulus intensity were defined [148].

Caloric reactions are especially interesting, since they are the result of separate labyrinth stimulation. A large set



/115

Figure 36. Vestibulograms of (A) a healthy human and (B) one suffering from chronic suppurative mesoepitympanitis, obtained from processing rotatory nystagmus ENG's (from [148]).

Stimulus -- positive acceleration $6.4^{\circ}\cdot sec^{-1}$ over 9.4 sec. X-axis -- time from beginning of rotation, sec (shown in 5-sec intervals within the limits of which nystagmometric characteristics were averaged); Y-axis -- averages for three characteristics of rightward (above the X-axis) and leftward (below the X-axis) reactions: (1) SC frequencies, sec^{-1}; (2) amplitudes, $^{\circ}$ and (3) their products, $^{\circ}\cdot sec^{-1}$.

of nystagmometric characteristics, including both traditional and new characteristics previously unused to describe reactions [128, 129], was studied. For practical purposes (particularly nystagmometric diagnostics), it is desirable to have a not very large, but adequate set of characteristics. The relationships of individual characteristics should be kept in mind in creating this sample. Nystagmus can hardly be described with adequate completeness if any one characteristic is considered (even in detail). Consequently, an integrated approach to quantitative evaluation of nystagmus is needed, i.e. simultaneous consideration of several characteristics, their comparison, and determination of the relationships among them [114, 364, 489, 544, 546]. Slow component amplitude, for example, should not be considered separately from SSC and nystagmus frequency, since the latter may vary relative to one another [118,

/116

121, 422, 555, 556]. Further, in selecting quantitative characteristics of vestibular nystagmus, we must keep in mind the dynamic nature of this reaction -- that it varies over time. Hence it is necessary to continue the search for and study of DC's and of possibilities for using them to describe the norm and for nystagmometric diagnostics.

One might say that the very choice of quantitative characteristics suitable for describing a normal reaction is a rather complex task. When, in diagnostic work, a nystagmogram taken separately is compared with a set of normal ENG's, the latter must be described statistically in terms of individual characteristics. In other cases (type 2 diagnosis), the tasks are different, since a pair of nystagmograms recorded from one subject with stimulation of different labyrinths is evaluated. Reactions from two labyrinths of a healthy human are not entirely identical: normally there is a certain asymmetry [228, 546]. Consequently, diagnosis in terms of the asymmetry indicator requires a somewhat different statistical description of the norm -- one which accounts for paired relationships of like characteristics (e.g. average frequencies for nystagmic reactions obtained by stimulating right and left labyrinths), since only this description will make it possible to compare differences in characteristics in a pair of reactions in a subject and the degree of asymmetry normally permissible.

Below are the definitions, terminology, and symbols which will be used later in presenting material.

Quantitative characteristics of vestibular nystagmus (or nystagmometric characteristics) include values which can be measured and are suitable to describe various nystagmus properties. /117

Characteristics are, first, the values which describe the properties of the reaction as a whole. For example: latent period (T_{lp}), reaction duration (T_R), number of nystagmic impulses (NI=N), total SC amplitude (ωA_{SC}).

Second, characteristics encompass the results of measuring individual nystagmic impulses. For example, the i-th nystagmic impulse can be described by the amplitude of the slow component (A_{SCi}); the duration of the slow component (T_{SCi}); slow component speed ($\omega_{SCi} = A_{SCi}/T_{SCi}$); amplitude, duration and speed of the fast component (respectively A_{FCi}, T_{FCi}, $\omega_{FCi} = A_{FCi}/T_{FCi}$); and the frequency value, which is the reciprocal of the duration of the nystagmic impulse ($F = 1/[T_{SCi} + T_{FCi}]$), where i includes all whole numbers from 1 to N.

Characteristics which describe a particular property of an individual nystagmic impulse can be referred to as elementary.

The sequence of elementary characteristics corresponding to the sequence of nystagmic impulses and reflecting the change in nystagmus over time is a dynamic characteristic.

A dynamic characteristic may be defined as a table showing the correspondence of values for a certain elementary characteristic to the position of a given nystagmic impulse on the time axis, on which zero is the point when stimulation of the vestibular apparatus begins. This table consists of two columns and N lines (N is henceforth equal to the number of impulses), or of N pairs (X_i, t_i), where X_i identifies the elementary characteristic X for the i-th impact, while t_i represents the time at which the impulse begins. The table can be transformed, for example, by averaging adjacent lines. This averaging can be done to make the time scale uniform. The entire time scale is divided into various intervals, and the characteristics of impulses within each interval are averaged. Another operation is to equate characteristic values (e.g. by sliding weighted mean), which makes it possible to significantly reduce noise level and produce a series which can be conveniently represented in the form of a curve.[1]

Dynamic quantitative characteristics can formally be interpreted as a table of values for a continuous time function X(t). These time functions, which correspond to like dynamic characteristics plotted for different ENG's, can be considered elements in a certain sample and can be averaged to produce a generalized picture of the dynamics of a particular characteristic. During averaging, each individual characteristic can undergo /118
preliminary rating (e.g. in terms of area or maximum). Averaging can be done conveniently in sequence within identical time intervals. Figure 37 depicts the result of processing 54 ENG's in terms of four characteristics (in this case, individual characteristics were not rated beforehand). To combine several different characteristics with different dimensions on the same graph, each of the previously averaged characteristics was
rated in terms of its maximum. Three characteristics from /119
those given in the figure (frequency, SSC, and DSC) require no explanation. The fourth, called the cumulative curve (CC) will be discussed later.

Research on dynamic characteristics shows promise for both theoretical and applied nystagmometry. The dynamic characteristic, i.e. the behavior of elementary characteristics taken separately has three components: 1) basic tendency, 2) low-frequency oscillations superimposed on the basic tendency, and 3) noise.

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1 Techniques for computer processing of nystagmometric material are described in [86] and later were used to study eye movements during reading [69] and during diagnosis of psychic condition [70].

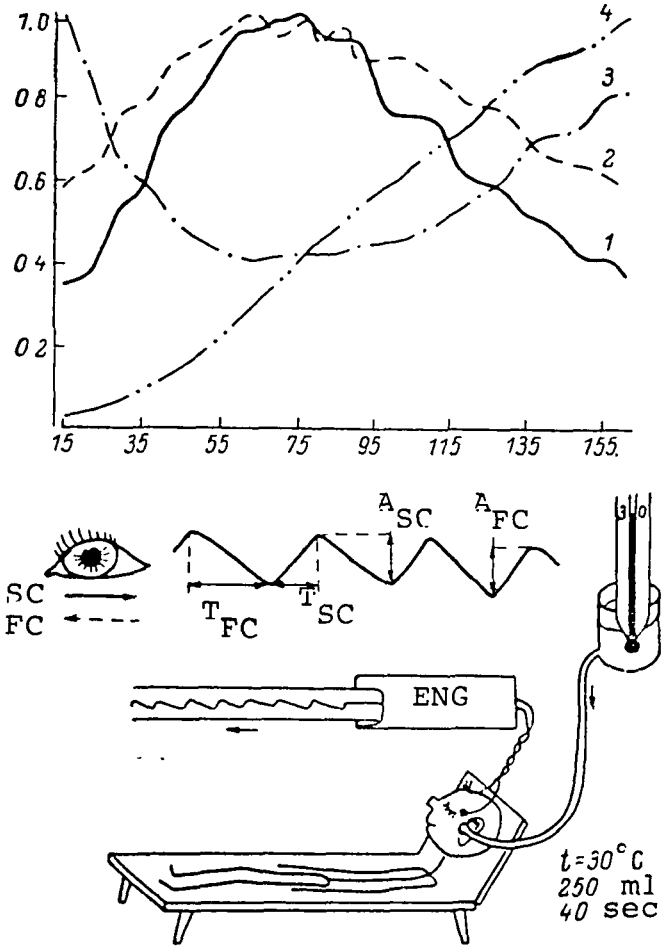

Figure 37. Dynamic characteristics of caloric nystagmus in man (averaged results of evaluating a sample of 54 cool reactions in 27 healthy humans) and a diagram of the caloric test (from [129]).

X-axis -- time from the onset of irrigation, sec; Y-axis -- norming in terms of DC maxima; (1) SSC, (2) frequency, (3) DSC, and (4) a cumulative curve.

Researchers noted the basic tendency before the other components, since it is apparently the one which most directly reflects the dynamics of cupuloendolymphatic displacement. For example, it has been shown that maximum caloric (cool) nystagmus frequency coincides in time with the highest level of cooling in the wall of the horizontal semicircular canal [389]. Low-frequency oscillations around the basic tendency are interesting because they resemble transient processes in tracking systems. Noise is apparently an unstable random process indicated by a change over time in the standard deviation of the parameters (if time axes are coordinated for various versions).

DC, as noted above, can be presented either as a table or as a graph. For example, it may be more convenient to use a

number reflecting a certain property of a graph, i.e. a functional rather than the graph itself to compare dynamic characteristics among themselves. Below are the meanings of a series of functionals for dynamic characteristics used to study caloric reactions and their formulas (for more detail, see [129]).

Arithmetic mean: $$\bar{X} = \frac{1}{N}\sum_{i=1}^{N} X_i.$$

where X is a certain DC for a reaction with latent period (T_{lp}), duration (T_R), and number of impulses (NI = N).

The interval average, i.e. the arithmetic mean characteristic for a given time (T_1, T_2):

$$X_{int} = \frac{1}{i_1 - i_2 + 1}\sum_{i=i_1}^{i_2} X_i.$$

where i_i and i_2 are the numbers of impulses located on the time axis closest to the interval's boundaries, i.e. to T_1 and T_2.

This study used an interval corresponding to a segment of the reaction extremum in most versions (T_1 = 30 sec; T_2 = 80 sec). Therefore, X_{int} can be considered equivalent to the maximum for the characteristic (or the minimum if a convex rather than a concave DC is involved, e.g. T_{SC}). /120

The interval average corresponds most closely to the so-called characteristic at the culmination segment, rarely mentioned in literature. The difference is that the latter usually does not denote the location and duration of the culmination on the time axis.

The two functionals under discussion are basically total characteristics, since they give a generalized evaluation of the reaction.

In addition, three functionals first used in quantitative description of nystagmus were used: $M_0(X)$, $M_1(X)$, and $M_2(X)$. Figure 38 explains the meaning of these functionals. Functional $M_0(X)$ is the area (shaded) limited by the curve x(t) and the time axis. The dimensionality of this functional naturally depends on the dimensionality of the dynamic characteristic X(t) and, in a specific instance when X(t) = SSC,

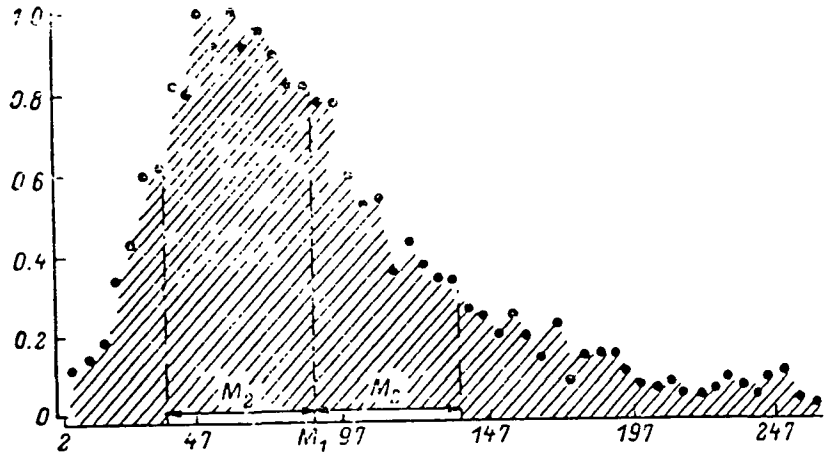

Figure 38. Dynamic characteristic of nystagmus and its functionals during evaluation of individual nystagmic reaction of a healthy human to a cool test (from [129]).

Graph of SC speed. X-axis -- time from beginning of nystagmus, sec. Y-axis -- SSC, normed in terms of the maximum. Points on the graph were obtained by averaging SSC at 5-sec intervals. The meaning of moments M_1, M_2 and M_3 (shaded area) is shown. The absolute values and dimensionality of the DC functionals $\omega_{SC} = 14^\circ \cdot sec^{-1}$, $\omega_{SCmax} = 40^\circ \cdot sec^{-1}$, $T_{max} = 72$ sec; $M_0 = 2685^\circ$; $M_1 = 87$ sec; $M_2 = 50$ sec; $T_R = 267$ sec; N = 301. Equations for calculating moments are:

$$M_0(X)=\int_0^{T_p} X(t)\,dt,\quad M_1(X)=\frac{1}{M_0}\int_0^{T_p} tX(t)\,dt,\quad M_2(X)=\sqrt{\frac{1}{M_0}\int_0^{T_p}(t-M_1)^2 X(t)\,dt},$$

where x(t) is the dynamic characteristic, T_R is reaction duration.

TABLE 13
MAIN TYPES OF NYSTAGMOMETRIC CHARACTERISTICS

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-/122

Name	Reflects	Purpose	Derived	Presented as	Example
Elementary (EC)	Parameters of individual (i-th) nystagmic impulse	Raw material for obtaining DC's and their functionals	Direct ENG measurment	Number	A_{SC_i} - SC amplit. of the i-th nystagmic impulse; T_{SC_i} -- SC duration of the same impulse $_{SC_i}$ -- SC speed of the i-th impulse
			Calculated from other EC's	"	
Dynamic (DC)	Change in subject nystagmus parameter over time	Compare reactions in different directions in one subject	From EC's of separate reaction	Table (or chart) showing correspondence of EC values to impulse position on time axis or correspondence of averaged EC's to averages for intervals on time axis	Graph of VPN SSC dynamics
		Compare reactions to stimuli of differing modalities	Others: average EC's in given time scale intervals, leveling norming		
		Identify tendencies in parameter changes	From DC sample (e.g. by averaging over given time interval segments	Table (or graph (of averaged DC's in terms of reaction sample	Graph of SSC dynamics for VPN sample
	Property of reaction as a whole	Compare reactions, formulate sets for statistical study	From individual nystagmogram	Number	T_{lp} - latent period, T_R - reaction duration, N - number of impulses A_{SC} - total SC amplitude
			From DC's	"	DC functionals: $_{SC}$ -- arithmetic mean for entire reaction; $_{SCint}$ -- interval for average; M_0 ($_{SC}$), M_1 ($_{SC}$), M_2 ($_{SC}$) -- moments

NOTES: 1. $M_{1(\omega SC)}$ and $M_{2(\omega SC)}$ have a time dimension. 2. $\bar{\omega}_{SCint}$ is an analog of SSC in the reaction culmination segment. 3. Functionals of the type $\bar{\omega}_{SC}$ and $\bar{\omega}_{SCint}$ represent the intensity class; the shape class includes $M_{1(\omega SC)}$, $M_{2(\omega SC)}$ and T_R; N and ΣA_{SC} belong equally to both classes.

functional $M_0(X)$ has amplitude dimensionality and corresponds approximately (but is not equal to) ΣA_{SC}. Functional $M_1(X)$ is the coordinate for the center of gravity for the flat figure limited by the curve for function X(t) and the time axis. In meaning, this is the first moment of function X(t), normalized by area, i.e. for the value of the functional x(t). Functional $M_1(X)$ has a time dimension. The next functional, $M_2(X)$, describes the diffuseness of the curve on the graph for function X(t) relative to a vertical line passing through the point with coordinates $M_1(X)$ and 0. This value is the square root of the second central moment of X(t), also normalized for area, i.e. for $M_0(X)$. /123

Functional $M_2(X)$ also has time dimensionality. Functionals $M_0(X)$, $M_1(X)$, and $M_2(X)$ were calculated by integration using the trapezium method. These functionals are suitable for most dynamic characteristics.

Just as mathematical expectation and dispersion describe the shape of the distribution density graph for a certain random function, $M_1(X)$ and $M_2(X)$ present a picture of the shape of the graph of the dynamic characteristic, making it possible to express the latter using a number.

Characteristics of this type, i.e. those which reflect time properties of a reaction or the shape of a graph, constitute a certain class of characteristics. Let us call this the shape class in contrast to the other class, that of intensity, having a priori assumed at this stage that two such classes exist. The validity of this division will be proven below in discussing relationships among characteristics.

Certain characteristics, formally functionals of dynamic characteristics, must nonetheless be included in the intensity class, not in the shape class, since they reflect reaction intensity. For example, functionals of the type ω_{SC} and ω_{SCint} reflect not so much the dynamics (shape) of a reaction, as the activity of the tonic system and, for this reason, are included in the intensity class.

Table 13 presents the result of an attempt to systematize nystagmometric characteristics.

Several comments are in order regarding the selection of characteristics by which nystagmus is to be evaluated in a particular instance of applied research on the vestibular function. Selection is not a simple matter, since the information value of the characteristic from the physiological and clinical standpoint (e.g. in the sense of tonic diagnostics) differs. Information value increases substantially if the characteristic's genesis can be correlated to the activity of any known physiological mechanism.

Statistical Study of the Norms of Caloric Nystagmus /124

The inadequacy of the caloric stimulus for the vestibular system is often stressed. However, literature still offers no description of facts which would force us to assume that the basic processes in the cupuloendolymphatic system during a caloric test differ from those during a rotatory test and that, in the norm, different structures and mechanisms take part in the formation of caloric or rotatory nystagmus. On the other hand, correlation of several characteristics indicates that the "inadequacy" of the stimulus is irrelevant for the resulting reaction, i.e. nystagmus. At the same time, caloric tests, in contrast to all others, offer so many more possibilities for research and give so much important data on the condition of the vestibular apparatus that they should be given priority within the system of vestibulometric studies.

Since any diagnostic research is somehow based on concepts of a norm, it is obviously necessary to describe this norm in sufficient detail. Creation of a generalized concept of normal nystagmic reactions to a specific stimulus is primarily a statistical task. This problem is solved in several stages: selecting nystagmometric characteristics, calculating these characteristics with an adequate amount of material, studying how they are distributed and the links among them, et al. Obviously, performing such work is virtually impossible without computers and flexible programming.

A sample of 54 ENG's (about 1500 nystagmic reactions) recorded in 27 humans was studied in detail [128, 129, 423]. The group of subjects comprised 16 men and 11 women aged 20 to 45. All underwent careful otorhinolaryngological examination beforehand and, as a result, none of the subjects had any sign of pathology in the middle or inner ear, nor was any detected in anamnesis nor during objective study (otoscopy, audiometry).

Caloric tests were conducted twice (on the right and on the left) with eyes closed. The subject was placed in supine position with his head raised 30° above horizontal. A liquid (nitrofurazone) at +30°C was fed in an amount of 250 ml from an ultrathermostat into the exterior auditory meatus over 40 sec. The test was done on the right ear first and, after an hour, on the left. Calibration, required to evaluate the ENG's, was done twice during each test (before irrigation and at the end of the nystagmus). A background EOG was recorded for each subject to eliminate spontaneous nystagmus. Nystagmography continued until the nystagmus stopped completely and subjective sensations disappeared.

Electronystagmograms were processed manually and each /125
nystagmic impulse was described by four elementary characteristics (A_{SC}, A_{FC}, T_{SC}, T_{FC}, measured in millimeters). The latent period was measured from the moment irrigation began un-

til the first nystagmus FC. The next stages were: input of numerical material into the computer, machine check of the quality of the material (by program), output of numerical material (for visual checking), correction of errors, and creation of a file on magnetic tape. The file was repeatedly accessed to formulate the required subsets during material processing. A "Dnepr-21" computer with a special program package was used to process the material [60, 61]. The latest development in an earlier set of programs in the language "MIR" [86], this package was written in the language "INF" [87].

Dynamic characteristic functionals, as well as T_{lp}, T_R, N and ΣA_{SC}, and a characteristic mentioned earlier -- extremum time (corresponding to the point on the time axis at which the subject dynamic characteristic [e.g. SSC] achieved maxima or minima [the latter applies, for example, to T_{SC}]) -- were studied by statistical variation method.

Table 14 presents the results of this processing. Each line describes a sample of characteristics comprising 54 ENG's. Arithmetic mean (x), root-mean-square deviation (σ), variation factor (CV), and the results of comparing an empirical sample with two theoretical distributions (normal and lognormal) are given for each characteristic.

Latent period (T_{lp}) has high variability (CV = 83%). It is possible that this is in part due to the difficulty of defining LP in terms of ENG. This high variability makes this characteristic useless in applied work, as indicated in literature [175].

Most characteristics vary over a rather wide range. The most stable characteristic (CV = 20%) is frequency ($\bar{F}$). This would seem to indicate that there is a certain optimum nystagmus rhythm for different subjects.

TABLE 14 /126

RESULTS OF STATISTICAL PROCESSING OF NYSTAGMOMETRIC CHARACTERISTICS (54 ENG'S DURING COOL TESTS ON 27 FAIRLY HEALTHY HUMANS) [129]

Characteristic and its Dimensionality	$\bar{x}$	σ	CV, %	$\bar{x}^L$	σ^L	p	
						normal	lognormal
T_{lp}, sec	7.14	5.95	85	1.51	1.07	-	0.114
T_R, sec	202.26	57.62	28	5.27	0.31	0.211	0.449
N	253.4	91.5	35	-	-	-	-
ΣA_{SC},°	2216	1234	56	7.54	0.59	0.307	0.670
$\bar{\omega}_{SC}$*	18.86	9.35	50	2.82	0.50	0.184	0.597
ω_{SCint}*	24.56	13.79	56	3.05	0.57	0.276	0.912

TABLE 14 (cont)

Characteristic and its Dimensionality	$\bar{x}$	σ	CV, %	$\bar{x}^L$	σ^L	p	
						normal	lognormal
$M_0(\omega_{SC})$, *	2946	1682	57	7.03	0.58	0.168	0.680
$M_1(\omega_{SC})$, sec	89.83	20.75	23	-	-	-	-
$M_2(\omega_{SC})$, sec	45.90	14.91	32	3.78	0.30	0.106	0.665
$\bar{F}$, sec^{-1}	1.94	0.39	20	-	-	0.752	0.580
$\bar{F}_{int}$, sec^{-1}	2.25	0.54	24	-	-	0.872	0.609
$M_0(F)$	302.8	104.2	34	-	-	-	-
$M_1(F)$, sec	94.72	24.50	26	4.52	0.26	0.117	0.247
$M_2(F)$, sec	50.53	16.83	33	3.87	0.34	0.361	0.421
A_{SC}, *	8.46	3.89	46	-	-	-	-
A_{SCint}, *	9.38	4.74	50	-	-	-	-
$M_0(A_{SC})$, $*\cdot sec^{-1}$	1654	876	53	7.27	0.55	0.081	0.813
$M_1(A_{SC})$, sec	100.23	24.70	25	-	-	0.210	0.029
$M_2(A_{SC})$, sec	52.92	15.76	30	3.93	0.30	0.168	0.257
$\bar{T}_{SC}$, sec	0.654	0.180	28	-0.50	0.26	0.175	0.333
T_{SCint}, sec	0.502	0.223	44	-0.80	0.36	0.001	0.364
$M_0(T_{SC})$, sec^2	184.81	88.54	48	-	-	-	-
$M_1(T_{SC})$, sec	118.38	38.57	33	-	-	0.175	0.124
$M_2(T_{SC})$, sec	60.52	16.89	28	-	-	0.504	0.363

*$\cdot sec^{-1}$.

NOTE: Arithmetic means and root-mean-square errors for raw ($\bar{x}$ and σ) and logarithmized ($\bar{x}^L$ and σ^L) samples; CV -- variation factor; p -- probability of error when the zero-hypothesis about the shape of the distribution is rejected.

The considerable variability of nystagmometric characteristics in the norm has often been noted in literature [228, 351, 545, 546] as has the fact that frequency varies comparatively less [546, 559].

Variation factors in functions of the type $M_1(X)$ and $M_2(X)$ were relatively small. This fact merits more detailed consideration. Since these characteristics were not studied before, it was natural to try to obtain indirect confirmation of the facts observed. This has been done by additional processing of the numerical material published in one study [398] on cool tests on healthy humans. Additional processing of this material made it possible to be sure that functions $M_1(F)$ and $M_2(F)$ are indeed characterized by low variability, and that this feature is preserved at two different stimulus intensities. /127

After the type of distribution has been defined, the zero-hypothesis is set as the assumption of affiliation with some type of distribution (normal or lognormal). Both zero-hypo-

theses were checked for each sample. The probability of error when the zero-hypothesis is repudiated (p) was calculated according to criterion χ^2 [180]. The zero-hypothesis was repudiated at p less than 0.05 (repudiation of the zero-hypothesis is denoted in table 14 by a dash). When p was greater than 0.95, the hypothesis was disregarded and it was assumed that so high a correlation was unlikely with limited experimental material. If experimental material appeared to correlate with both hypotheses, then preference was given to the one whose repudiation is associated with high probability of error (underlined in the table). When it was impossible to repudiate the hypothesis of affiliation with lognormal distribution, logarithms of the sample were taken and the arithmetic mean and root-mean-square deviation were also found for the transformed sample ($\bar{x}^L$ and σ^L).

Correlation with the hypothesis that distribution was normal in form was obtained only for a small part of the entire set of nystagmometric characteristics (e.g. $\bar{F}$ and $\bar{F}_{int}$). In most cases it was not the characteristics themselves, but their logarithms, which exhibited normal distribution. A certain portion of the characteristics (e.g. N, $\bar{A}_{SC}$, $\bar{A}_{SCint}$) could not be classified as either normal or lognormal in their form of distribution. Histograms (fig. 39) demonstrate certain empirical distributions obtained in comparison with corresponding histograms for theoretical series.

Of what significance are concepts of the type of nystagmic characteristics distribution? It might be that such a concept will be useful in theoretical work related to modeling the vestibular function. In particular, in several cases the lognormal form of distribution may mean that, in the subject system, the logarithm was recorded rather than the characteristic itself and, consequently, the logarithm of the characteristic during study of a system is more informative than the absolute value of the characteristic itself.

Determination of the type of characteristic distribution also has applied significance. It makes it possible, for example, to justifiably use Student's statistical criterion, which is used quite widely in biological research. Using this criterion is completely justified when the subject value is normally distributed. If two groups of ENG's are being compared, a characteristic whose distribution is subject to lognormal law must be used and, to avoid errors, logarithms, not absolute values of the characteristics, should be compared.

Literature devoted to vestibular nystagmus contains no direct studies concerning the type of nystagmometric characteristic distribution. However, further processing of certain published numerical materials has made it possible in some cases to establish the type of distribution. In particular,

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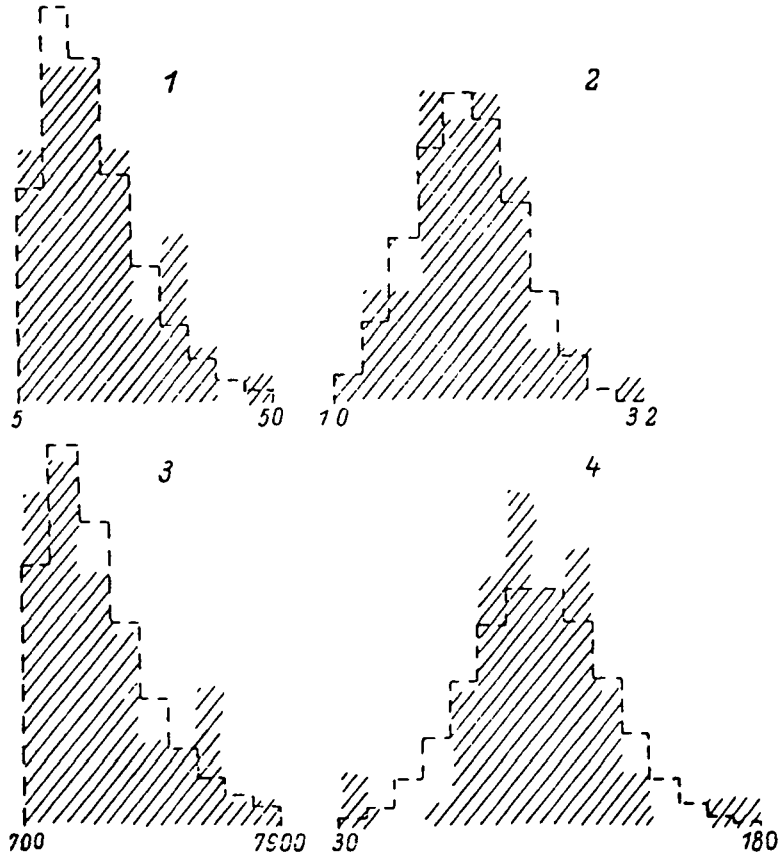

Figure 39. Types of distributions for dynamic characteristic functionals. The result of processing a sample of cool reactions (54 ENG's) (from [129]).

Histograms of empirical distributions (shaded) of four functionals: 1 -- $\bar{\omega}_{SC}$ = 18.86±9.35 ($\bar{x}\pm\sigma$ of the original sample); and 2.82±0.50 ($x\pm\sigma$ of the sample's logarithms), lognormal distribution, p (probability of error during confirmation of the difference in compared distributions -- empirical and hypothetical, shown by broken lines) = 0.597; 2 -- F = 1.94±0.35 (of original sample), normal distribution, p = 0.752; 3 -- $M_0(\omega_{SC})$ = 2946±1682 (of original sample) and 7.83±0.58 (sample logarithm), lognormal distribution, p = 0.680; 4 -- $M_1(A_{SC})$ = 100.2±24.7 (of original sample), normal distribution, p = 0.210.

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the arithmetic mean of "slow component duration" [162] has turned out to have a lognormal distribution (error in turning the hypothesis p = 0.854), duration of the reaction and "maximum eye speed" [545] (p = 0.903 and 0.334 respectively). It was also possible to formulate a sample similar to sample F described above with published numerical information [545] (cf. table 14). In this case the following correlation was observed: average frequency during positive angular acceleration

turned out to have normal distribution. Experimental data on caloric nystagmus [129] correlated quite satisfactorily with data obtained by further processing of published numerical material related to rotatory tests. This correlation made it possible to conclude justifiably that the type of characteristic distribution is not a function of the specific stimulation technique (caloric or rotatory), i.e. it is to some degree a universal property. If we take into account the fact that the primary nystagmometric characteristics in samples of nystagmic reactions obtained in experiments on rabbits [24] were distributed just as in humans, then it is natural to conclude that the mechanisms by which nystagmus develops in man and in rabbits are quite similar.

Definition of the type of characteristic distribution facilitated a correct approach to calculating correlation coefficients and confidence intervals for lognormal distributions (more about this below). Finally, the hypothesis on the type of distribution had to be tested to substantiate the feasibility of plotting multidimensional normal distribution, in order to approximate common distribution of three characteristics by three-dimensional normal distribution, which will be discussed in more detail below.

Relationship among Characteristics of Nystagmic Reactions. Statistical Relationships

Coefficients of linear correlation (r) and their 95% confidence intervals (r_1 and r_2) were calculated during research on the relationships between characteristics. Fisher's transformation was used for this purpose [30]. Figure 40 shows examples of correlation fields obtained in paired presentation of samples of various characteristics. Table 15 presents the summary result. With lognormal distribution, a sample of natural characteristic logarithms was selected to calculate r. For example, the procedure during study of the correlation in the pair $\bar{F}$ and $\bar{\omega}_{SC}$ was to calculate the coefficient of correlation between the absolute values of $\bar{F}$ and the logarithms of $\bar{\omega}_{SC}$. Table 14 denotes these cases with the symbol L. If the distribution differed from normal and lognormal (e.g. $\bar{A}_{SC}$), it was necessary to approach the sample just as with normal distribution.

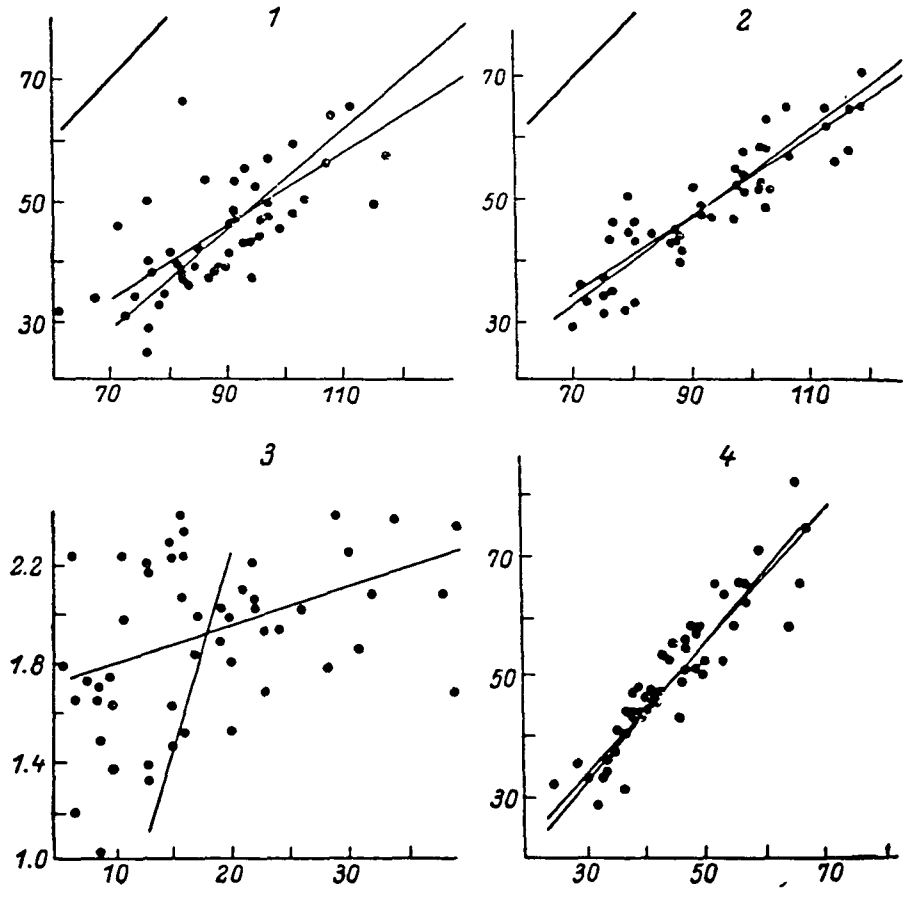

Figure 40. Correlation of various functionals (M_1 and M_2) of similar DC's -- (1) ω_{SC} and (2) F and identical functionals -- (3) $\bar{X}$ and (4) M_2 for different DC's (ω_{SC} and F) (from [129]).

X-axes -- on 1: $M_1(\omega_{SC})$, sec; on 2: $M_1(F)$, sec; on 3: $\bar{\omega}_{SC}$, $\cdot\cdot sec^{-1}$; on 4: $M_2(\omega_{SC})$, sec; Y-axes -- on 1: $M_2(\omega_{SC})$, sec; on 2: $M_2(F)$, sec; on 3: $(\bar{F})$, sec^{-1}; on 4: $M_2(F)$, sec.

Regression lines are shown. Values of regression coefficients ($R_{x/y}$ and $R_{y/x}$) are equal to 1.193 and 0.0616 (on 1), 1.394 and 0.658 (on 2), 8.609 and 0.015 (on 3), 1.086 and 0.862 (on 4) respectively. Thick lines (in 1 and 2) indicate bisectors of coordinate angles.

Correlation was, of course, complete when characteristics were known to be related. However, in several cases a high correlation was noted also when the relationship between characteristics could not be explained only as the result of the procedure by which the characteristics themselves were calculated.

Let us consider the correlation between characteristics belonging to the same system, for example to the tonic system whose condition should be reflected in SSC. The existence of /131

TABLE 15. CORRELATION BETWEEN NYSTAGMOMETRIC CHARACTERISTICS (54 ENG's DURING COOL TESTS ON 27 VIRTUALLY HEALTHY HUMANS) [129]

Samples Compared	Linear Correction Coefficient	Boundaries of 95% Confidence Intervals	
	r	r_1	r_2
T_p^L-N	0.682	0.507	0.803
"-ΣA_{SC}^L	0.460	0.219	0.648
"-ω_{SC}^L	-0.016	-0.283	0.252
"-$\bar{\omega}_{SC}^L$	-0.076	-0.337	0.195
"-ω_{SCint}^L	0.854	0.776	0.919
"$M_1^L(\omega_{SC})$	0.912	0.852	0.948
-$\bar{F}$	0.005	-0.263	0.272
-$\bar{F}_{int}$	0.059	-0.212	0.321
-$M_1^L(F)$	0.961	0.934	0.978
-$M_2^L(F)$	0.971	0.950	0.983
N-ΣA_{SC}^L	0.628	0.433	0.767
-$\bar{\omega}_{SC}^L$	0.318	0.055	0.540
-ω_{SCint}^L	0.022	-0.247	0.288
-$M_1(\omega_{SC})$	0.499	0.267	0.676
-$M_2^L(\omega_{SC})$	0.527	0.302	0.686
-$\bar{F}$	0.626	0.430	0.766
-F_{int}	0.133	-0.140	0.387
-$M_1^L(F)$	0.627	0.432	0.766
-$M_{SC}^L(F)$	0.639	0.448	0.774
ΣA_{SC}-$\bar{\omega}_{SC}^L$	0.836	0.733	0.902
-ω_{SCint}^L	0.206	-0.065	0.449
-$M_1(\omega_{SC})$	0.307	0.042	0.531
-$M_2^L(\omega_{SC})$	0.373	0.117	0.582
-$\bar{F}$	0.278	0.011	0.508
-F_{int}	0.033	-0.286	0.298
-$M_1^L(F)$	0.369	0.112	0.579
-$M_2^L(F)$	0.420	0.172	0.618
$\bar{\omega}_{SC}^L$-ω_{SCint}^L	0.327	0.065	0.547
-$M_1(\omega_{SC})$	-0.135	-0.389	0.137
-$M_2(\omega_{SC})$	-0.099	-0.357	0.173
-F	0.408	0.157	0.609

TABLE 15 (cont) /132

Samples Compared	Linear Correction Coefficient	Boundaries of 95% Confidence Intervals	
	r	r_1	r_2
$\overline{\omega}^L_{SCint}$-$M_1(\omega_{SC})$	0.077	-0.338	0.194
"-$M^L_2(\omega_{SC})$	-0.120	-0.376	0.152
"-$\overline{F}_{int}$	0.520	0.292	0.691
$M_1(\omega_{SC})$-$M^L_2(\omega_{SC})$	0.862	0.773	0.918
"-$M^L_1(F)$	0.926	0.874	0.956
"$M^L_2(F)$	0.872	0.888	0.924
$M^L_2(\omega_{SC})$-$M^L_1(F)$	0.896	0.827	0.939
"-$M^L_2(F)$	0.952	0.918	0.972
$\overline{F}$-$\overline{F}_{int}$	0.262	0.005	0.495
"-$M^L_1(F)$	-0.037	-0.301	0.233
"-$M^L_2(F)$	-0.061	-0.324	0.210
$\overline{F}_{int}$-$M^L_2(F)$	0.102	-0.170	0.360
"-$M^L_2(F)$	0.045	-0.225	0.309
$M^L_1(F)$-$M^L_2(F)$	0.951	0.927	0.971

NOTE: Samples for which logarithms are taken are indicated by the letter "L."

relationships among characteristics in the intensity class, i.e. between ω_{SC} and ω_{SCint} was clearly revealed. The shape class also exhibited clearly pronounced correlations; for example between $M_1(\omega_{SC})$ and $M_2(\omega_{SC})$. These connections are trivial. The definite lack of correlations between characteristics of different classes is more interesting. For example, there is no correlation between $(\overline{\omega}_{SC})$ and $M_1(\omega_{SC})$; (ω_{SC}), and $M_2(\omega_{SC})$, etc. It is precisely these relationships which were identified between characteristics of rhythmic systems, presented as frequency characteristics: characteristics are closely related within classes, but there are no connections between classes. For example, in the shape class, $M_1(\omega_{SC})$ and $M_1(F)$, $M_1(\omega_{SC})$ and $M_2(F)$, etc. correlate. Similar relationships take place within the intensity class.

Characteristics comprising, as it were, an intermediate link between two classes (including $M_0(\omega_{SC})$ and ΣA_{SC} which is close in meaning, as well as $M_0(F)$ and N) turned out to correlate strongly not only among themselves, but also with concepts in both classes.

The most important fact observed during study of correlations is the definite absence of relationships between characteristics which represent different classes. It has been proposed that these classes are statistically independent. This /133

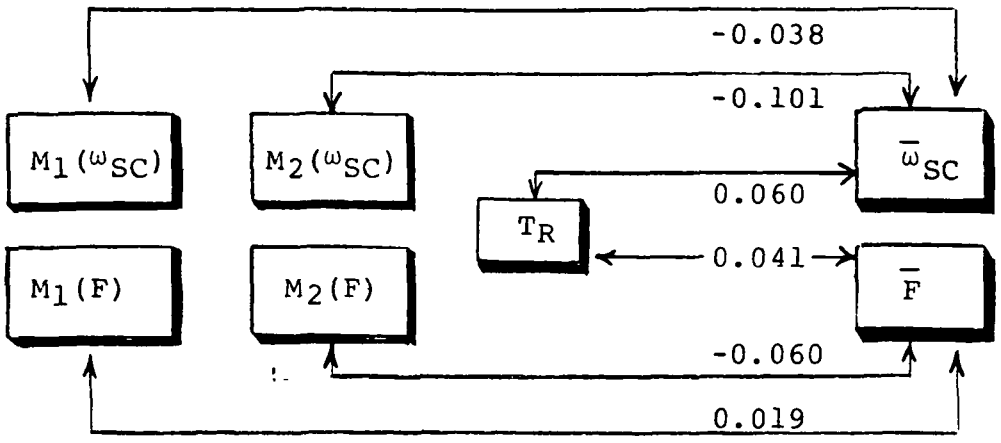

Figure 41. The result of testing the hypothesis that nystagmometric characteristics belonging to different classes -- shape (left group) and intensity (right group) are independent (from [129]).

Arrows indicate pairs of characteristics samples; numbers -- the values of Spearman's ranking correlation coefficients (R). The hypothesis that a sample of given size (54 ENG's) for a given level of significance (less than or equal to 0.05) is independent can be repudiated if the absolute value of R is greater than 0.3.

hypothesis was tested by using Spearman's nonparametric criterion [30]. The hypothesis of independence could have been repudiated at an absolute value of R greater than 0.3 (R being Spearman's ranking coefficient; the level of significance was less than or equal to 0.05, sample size -- 54).

Figure 41 shows the results of the test. Clearly, when paired samples from different classes are compared, functionals of dynamic characteristics higher than those belonging to different classes (e.g. ω_{SC} and $M_1(\omega_{SC})$, $\bar{F}$ and $M_2(F)$, etc.) can, in all cases, actually be considered independent. There was a statistically certain lack of relationship (coefficient $|R|$ was less than 0.3, and its limits were from 0.019 to 0.101).

It is also interesting to note that T_R turned out to be in the shape class, since it reliably correlates with representatives of that class, while, in contrast, there was no reliable relationship with characteristics of the intensity class. The question to which class T_R belongs is not a formal one, since reaction duration is often used in practice to assess nystagmus intensity (cf. e.g. [147]). This point of view should apparently be rejected, since we have obtained definitive confirmation of S. M. Kompaneyts' opinion, which was formulated on the basis of analyzing literature almost half a

century ago, when nystagmus duration was still the only nystagmometric characteristic used in practice: "...Nystagmus duration cannot be exclusively the expression of peripheral vestibular apparatus stimulation; it is also the expression of the activity of corresponding centers in the brain" ([89], p. 540).

Table 15 does not contain T_{1p}, since it was discovered that this characteristic does not correlate with any of the other characteristics. This fact merits attention in and of itself, since it casts doubt on the value of T_{1p} for diagnostic research.

To summarize this discussion of the relationships between nystagmometric characteristics, we can note that establishing correlations between characteristics makes it possible, first, to eliminate excess in describing the norm. Second, it is quite useful to compare the correlation between individual characteristics in the norm and in a pathology. If, given a pathology, the nature of the relationship changes, then it would be advisable to make use of this fact in diagnostics. This assumption is not without basis. In particular, in an experiment on cats [362], after unilateral delabyrinthation it was observed that coefficients of linear correlation between OKN characteristics are different in reactions obtained with optokinetic stimulation in different directions. This means that, under different experimental conditions and with different forms of pathology, correlation coefficients in and of themselves can acquire diagnostic significance. Third, discovery of relationships between various characteristics is important in solving problems related to modeling. Fourth and finally, calculating correlations is neccessary for subsequent use of these results to calculate combined probability density. /134

Correlations between characteristics, just as the type of characteristic distribution, are apparently not a function of the type of stimulation (caloric, rotatory). This is demonstrated by comparing the data given above with certain other information from literature. For example, a significant correlation between F and SSC was noted during a caloric test on a human, although it weakened somewhat as stimulus intensity increased [558, 559]. A correlation between F and SSC which did not vary if angular acceleration changed was also noted in studies on cats during rotatory tests [364].

Naturally, we have been unable to find published data on previously unused characteristics (functionals of the type $M_1(X)$ and $M_2(X)$), i.e. on typical representatives of the shape class. However, certain analogs can be found. For example, in several cases, the correlation of particular characteristics with nystagmus duration was studied (remember that T_R belongs to the shape class). Caloric tests on humans [544] showed that the number of impulses and intensity (the latter was

determined similarly to ω_{SCint}) correlate positively, while T_R does not correlate with these characteristics. It was also possible to obtain certain information in relation to rotatory tests. Simple recalculation of published numerical data [545], for example, made it possible to establish that $\bar{F}$ does not correlate with T_R ($r = -0.105$, $r_1 = -0.394$, $r_2 = 0.153$). Thus it was possible to confirm that the nature of correlations is not a function of stimulus adequacy.

The problem of two classes of characteristics is just as important. It has been possible to ascertain that they sxist by using a formal approach. Understandably, it is still impossible to assert that the lack of correlation between characteristics of the shape class and characteristics of the intensity class is a universal phenomenon, i.e. inherent in a wider range of vestibular reactions, not just in cool nystagmus, which /135 has been studied in specific experimental situations [128, 129].

If these classes are actually autonomous, then one might expect that they would behave differently in certain experimental conditions. The validity of the assertion that they are autonomous can be indirectly confirmed by the fact that characteristics belonging to different classes undergo different changes as they weaken to repeated vestibular stimulation [114, 228, 274], as well as due to combined stimulation of the semicircular canals and otoliths [173].

In particular, an article devoted to the study of the weakening reaction of caloric cool nystagmus in humans [274] showed that different characteristics behave differently depending on experiment conditions. One detail which seems significant from the standpoint of the assumptions discussed above was revealed. Repeated calorization led to changes in characteristics such as the number of impacts (in experiments in darkness), and total amplitude (in experiments with vision fixed), but did not affect reaction duration.

An article devoted to finding an integrated quantitative characteristic of nystagmus which would simultaneously reflect the behavior of both the slow and fast components of nystagmus [114] used so-called average harmonic velocity. Specifically, it was found that, when vestibular rotatory nystagmus weakens, the number of impacts and the absolute value of the slow component's velocity, again a characteristic of the intensity class, decreases, while the shape of the curve for average harmonic velocity is preserved.

Characteristics of the shape class are apparently not as directly dependent on stimulus magnitude as are other characteristics. This might be related in part to the fact that an increase in angular acceleration during repeated rotatory tests is not accompanied by a substantial change in reaction duration, while the number of impulses increases substantially. In

other words, nystagmus duration is not a function of stimulus intensity, while frequency is very much so [207].

This then means that, in the norm, changes in intensity class and shape class characteristics caused by stimulus features are not parallel: if the the intensity class varies noticeably, the shape class varies little or not at all. Naturally, when vestibular dysfunction is being identified, characteristics representing different classes may behave differently depending on the nature and localization of the injury. The two classes of nystagmometric characteristics reflect different properties (and mechanisms) of nystagmus. Since characteristics of the two classes are not related, the shape and intensity /136
of a reaction are relatively independent properties of vestibular nystagmus and the primary features of the classes are apparently preserved during different type of stimulation (caloric test, rotatory test) and exist both in man and in other mammals (rabbits, cats).

Studies of statistical relationships have made it possible to draw two conclusions: 1. In the norm, any two characteristics of nystagmus belonging to different classes vary independently when the stimulus is the same. 2. Within each class there are, in the norm, close statistical relationships between characteristics, regardless of the activity of whichever of the two systems involved in developing nystagmus (tonic or rhythmic) is reflected by these characteristics.

These conclusions make it possible to formulate the following hypothesis: VN develops in at least two directions: through development of reaction intensity and through development of "shape" (dynamics). Two different mechanisms, functioning relatively independently, are involved.

The Problem of Symmetry of Normal Vestibular Nystagmi

Since one of the cardinal problems in diagnostic research is the functional symmetry of the two vestibular apparati, and since the primary indicator by which this symmetry is evaluated is nystagmus, it is quite important to understand how symmetrical, in the norm, are nystagmic reactions caused by a single stimulus applied to different labyrinths.

If nystagmograms for right- and leftward tests on a healthy human are compared, they can be differentiated to a certain extent in terms of several characteristics. This difference may have two causes. The first is actual asymmetry, a stable change in the reactivity of one labyrinth. In this case, repeated studies under similar conditions reveal that, in all cases, the reaction in the same direction prevails. The second possible cause is that the vestibular system, like all other paired systems, is somewhat unstable, i.e. fluctuations in the balance between right and left sides occur systematically. In

contrast to the asymmetry noted above, in this case, when studies are repeated, the probability that right or left nystagmus will dominate will be close to 0.5 and the result will be depend on in which phase of oscillation the study was done.[1]

Vestibular asymmetry is a rather complex problem and, /137
despite several publications, unquestionably requires even more specialized study. An attempt to solve a particular problem -- to describe statistically the differences between caloric reactions of different labyrinths during the same test -- was made using cool nystagmus [129]. This description is necessary so that, once the difference in patient reactions during the study has been described, it can be evaluated by comparison with differences which occur in the norm.

In a study of symmetry (actually asymmetry) a sample consisting of pairs of reactions was considered. Each pair of ENG's was recorded in an individual subject during cool tests from right to left. Relative asymmetry was calculated for each pair of ENG's. A formula of the following type was used:

$$\Delta C = [2(X_r - X_l)/X_r + X_l] \cdot 100\%$$

where ΔC is the modulus of relative asymmetry, %, and X_r and X_l are individual identical nystagmometric characteristics, obtained during right- and leftward tests. We can limit ourselves to certain summary remarks on the results of this study. It was revealed that, in the norm, asymmetry can be rather significant. For example, the arithmetic mean for the modulus of asymmetry in terms of ω_{SC} equaled 39.4% and in terms of $\bar{F}$, 16.4%. It turned out that asymmetry is generally more typical for characteristics of the tonic system than for those of the rhythmic system. Characteristics of the shape class were more symmetric then those in the intensity class. Variation $M_1(F)_1 > M_1(F)$ occurred twice as often as the reverse. This was also the case in terms of $M_1(\omega_{SC})$, i.e. in dynamic characteristics obtained during a cool test on the left, the coordinate of the center of gravity of a flat figure defined by the time axis and the DC curve somehow lagged behind. Approximately similar data were obtained for both $M_2(F)$ and for $M_2(\omega_{SC})$.

The difference among results of cool tests from right to left in the same subject in the sample considered cannot be interpreted equivocally. Bear in mind that right-side tests precede left-side tests and that the sequence of tests does make a difference. There are, for example, indications that the result is less reliable in the first of four caloric BT

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1 Anatomical causes are also possible, e.g. caloric nystagmi may be asymmetric due to differences in pneumatization of the temporal bone.

tests. Therefore it was proposed to conduct five tests and disregarding the first. However, the diagnostic value of defining asymmetry in terms of a monothermal caloric test is even more problematic for another reason. The fact is that asymmetry observed in a monothermal test can be considered only as a sign of pathology, nothing more. It cannot be used to draw conclusions on the existence of a difference in labyrinth reactivity, on which side is injured, etc. Obtaining more or less complete information requires data on thermal reactions. Finally, note that, even if there is no asymmetry (according to data from a monothermal test), it is also impossible to exclude pathology. These assertions will be understood after chapter 4. /138

Certain Nontraditional Nystagmometric Characteristics

We will attempt to determine the prospects of using certain nontraditional characteristics. Functionals of the type $M_0(X)$, $M_1(X)$, and $M_2(X)$ may offer promise in diagnostic, as well in the study of adaptation, habituation, and the effect of extralabyrinthine and other factors.

DC's which make sense as accumulation graphs or cumulative curves are of unquestionable interest. Since the slow (tonic) and fast (phase) components of nystagmus are caused by different systems [110, 113, 143-145], it makes sense to find characteristics which, in isolation, reflect the behavior of each system. For the phase system, which can be considered as setting nystagmus rhythm, graphs are proposed with coordinates for time and number of impulses. These graphs reflect a certain total which increases over time.

The cumulative curve has special significance in studying the tonic system, since elimination of the fast component makes it possible to represent system activity in its pure form [118].

This question should be dealt with in more detail. Two systems participate in the development of nystagmus -- one forms the tonic component; the other fragments the tonic reflex, disturbing this reflex in the nystagmus itself. Each system is closely related to the activity of the vestibular apparatus and to the level of afferentation. At the same time they are relatively independent in the sense that changes in one system may not be connected to changes in the other [110, 112, 113]. Nystagmic impulse SSC's are fragments of the tonic reflex. Therefore, the first system can be called the SC system. The tonic reflex is transformed into a rhythmic reflex by virtue of the fact that the second system (the FC system), related more or less regularly, interrupts the tonic reflex for a brief time and organizes rapid eye movement in the opposite direction. Then the FC system seems to disconnects for a time, making it possible for the SC system to produce a slow turn in the next nystagmic impulse. The mechanism of nystagmus is actually much more complicated. However, in this case, no /139

further detail is required. What is important is that there are two systems and that it must be assumed that the first (SC system) can function only independently, in which case there is no nystagmus (there is only a tonic reflex), or in interaction with the second (FC system), which results in nystagmus.

Many properties of nystagmus depend on the FC system's level of activity. Frequency more than any other is a function of this activity, since it is determined by the duration of the nystagmic impulse, and the latter is composed of the durations of its slow and fast components. We must emphasize: nystagmus frequency depends not only on time taken by SC, but on how long it takes for the impulse to end entirely, i.e. for the FC system to shut down.

Further, the FC system to a certain extent determines ASC: if, for example, SC speeds for a certain portion of nystagmus are identical, SC amplitudes cannot be identical: the more active the fragmenting system, the smaller the amplitudes. Finally, FC system activity determines whether the eye returns to its initial position at the end of nystagmus. During nystagmus, eye movements do not always occur near the point corresponding to a direct gaze. Most often there is a certain "drift," a relatively slow shift building up from impulse to impulse. Similarly, this phenomenon to a great extent depends on FC system activity: if activity is insufficient, the shift will be toward the SC; if it is excessive, toward the FC. Thus the condition of the FC system has a profound effect on features of a particular reaction. At the same time, the condition of the FC system itself is determined not only by the level of vestibular afferent flow, as has been shown by physiological experiments [107, 109, 110, 112, 113], but by several other factors. We must emphasize that the changes expressed may have an entirely nonvestibular origin [556]. In other words, not every change in nystagmus characteristics caused by deviations in the FC system is a sign of vestibular dysfunction. Therefore, in several cases, it is useful to use a dynamic characteristic such as CC, which quite thoroughly reflects the status of the SC system, but at the same time is not completely dependent on the status of the FC system, since the influence of the latter is artificially eliminated [118].

Figure 42 shows the mechanism for plotting such a graph to reflect eye movement trajectory, provided that there are no restrictions to movement. A nystagmogram of a rabbit was recorded by photonystagmometric procedure [140]. The horizontal component of prolapse nystagmus (the result of surgical interference at one horizontal canal), was directed toward the untreated labyrinth. Subsequent changes in nystagmus took place /140
due to stimulation of perforated lateral canal receptors (a series of rectangular electrical impulses lasting 0.2 msec and occurring at a frequency of 60 imp/sec.) by a bipolar electrode introduced into the ampulla [110]. Prolapse nystagmus was re-

placed by stimulation nystagmus. Three sections of the nystagmogram were distinguished by several features caused in part by FC system activity. Nystagmus frequency differed in impacts per second: on the left -- 3; in the middle -- 4.5; and on the right, about 2. And, in the middle section, corresponding to the period of electrical stimulation, the eye noticeably drifted in the direction of the SC. When stimulation ended, the

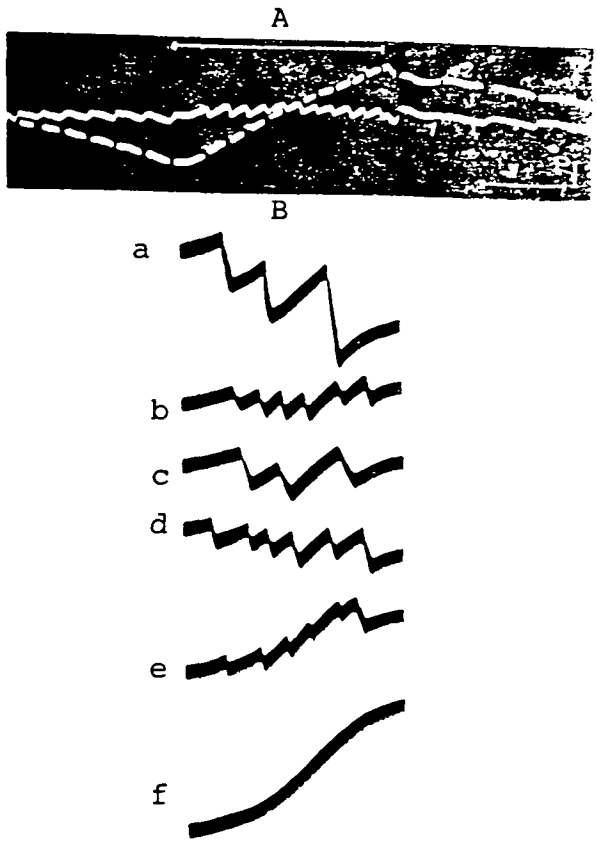

Figure 42. Cumulative curves for: (A) nystagmus in a rabbit, (B) a series of conventional nystagmograms, and (C) caloric nystagmus in a human (from [118]).

A -- (1) Photonystagmogram, compiled with a (2) CC plotted by hand (horizontal line upward denotes rhythmic electrical stimulation of the ampullar receptor; calibration: 10°, 1 sec). Prolapse nystagmus (left part of the recording) is replaced by stimulation nystagmus and is then restored. Changes in the status of the SC system are quite clear on the CC. B -- A series of conventional nystagmograms (a-e), plotted on the same time-scale, have a common CC for all nystagmi (f). C -- graph for CC obtained during computer processing of human ENG's. X-axis -- time from beginning of nystagmus, sec; Y-axis -- cumulative curve, °.

C

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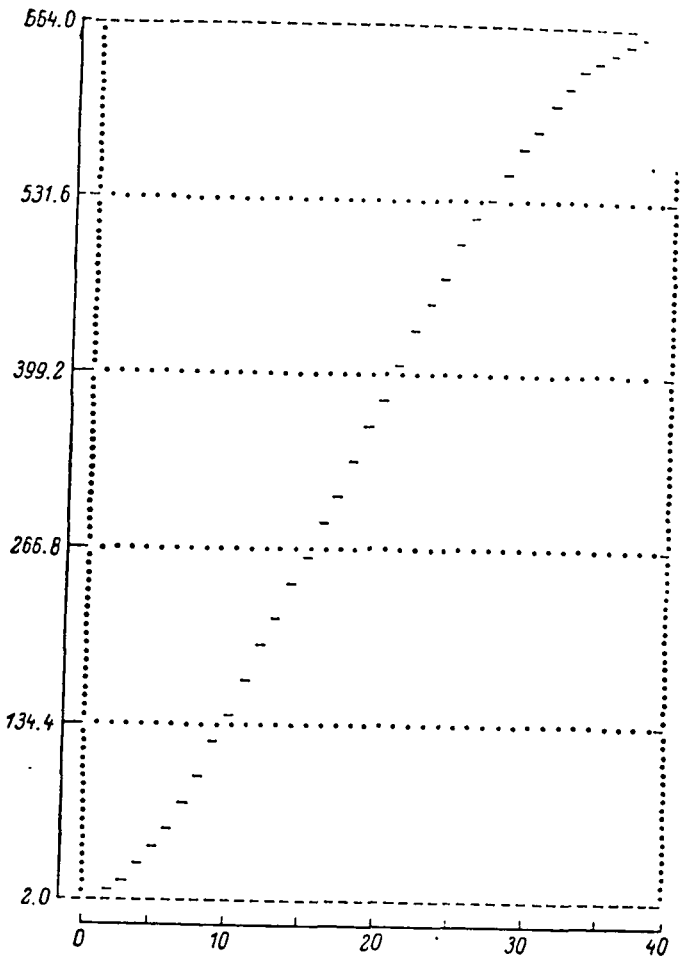

Figure 42 (cont)

last two impulses (of those belonging to stimulation nystagmus) turned out to be not entirely standard in shape: in the first FC lasted longer than SC; in the second, the beginning of SC was preceded by a high-speed jump. In other words, the reaction can be considered sufficiently complex in shape. The same figure shows the result of special processing of this nystagmogram: all sections corresponding to fast components were removed (literally cut out). Fragments of the recording corresponding to slow components were preserved in the earlier segments of the time scale, but each was shifted vertically until it began to approach an imaginary line which is the result of extrapolating the preceding SC. As a result of this transformation, which involved sequential shifting of all slow components, the components turned out to be stretched into a chain and arranged in a line, as if continuing one another. Each SC retained its former slope. If the gaps corresponding to the excluded FC's are filled in, i.e. if eye movement is represented /142
as continuous, we can state that the result is the graph of a freely occurring eye movement caused only by the activity of

the tonic system. The shape of this graph, which has path-time coordinates, depends on processes taking place in the SC system and caused by disruption of the balance between right and left vestibular nuclear complex activity levels. Artificial exclusion of the effect of the FC system made it possible to make the three periods of SC system activity more obvious. If the cumulative curves were continued to the left, then slope at a considerable distance would remain unchanged due to the monotony of the prolapse nystagmus (preponderance of the activity of the vestibular nuclear complex on the untreated side). The middle portion, corresponding to the electrostimulation period, when prolapse nystagmus slowed almost instantaneously and stimulation nystagmus in the opposite direction occurred, is interesting. SSC (tangent of the slope of the curve) during this entire stimulation period remained constant. After stimulation ceased, spontaneous prolapse nystagmus was restored after about 1 sec, the speed of its SC increased gradually, and a significant amount of time was required for it to stabilize. SSC did not stabilize within the limits of the fragment shown in the drawing.

In everyday practice, these cumulative curves are now produced by computer along with several other dynamic characteristics. This method is not as time-consuming as that described above. Each interval corresponding to FC is filled in by linear extrapolation of the previous SC, i.e. when the curve is plotted, it is assumed that an eye version angle equal to $A_{SC} + (\omega_{SC} \cdot T_{FC})$ corresponds to each time segment equal to the duration of the next nystagmic impulse ($T_{SC} + T_{FC}$). As a result, involvement of the FC system is somehow eliminated. Instead of nystagmus, a hypothetical reaction whose origin is due only to the tonic system is considered. The steepness of the slope of the curve (cf. figure 42 B) can be used to judge the rate of eye movement at separate stages of the reaction, while its S-shape during, for example, a caloric test results from the fact that SSC increases when nystagmus begins, but decreases again as it ends. In essence, the curve reflects a certain potential capacity of the SC system, i.e. the range of movements which this system can bring about upon exposure to a given stimulus. In other words, the curve reflects not just a clear actual movement, but also latent, unrealized capacities (by virtue of the FC system). The maximum level reached by the curve is closest in meaning to the sum of slow component amplitudes, but in terms of absolute value is somewhat greater, since it contains "unrealized movement" at those time segments where actual movements (i.e. FC's) in nystagmus were opposite in direction. The graph for the cumulative curve can be considered a successful reflection of the energy state of the FC system (i.e. of the tonic vestibulo-oculomotor reflex) which, in turn, is determined by the status of the vestibular apparati. Any FC system influence on this characteristic is prevented. This /143
dynamic characteristic, like others discussed above, can be expressed by a functional. The steepness of the curve's slope,

which has a dimension of angular velocity, can be taken as a functional.

From a mathematician's viewpoint, CC contains no additional information when compared, for example, to the dynamic characteristic of SSC. However, it is useful in the didactic sense. One can be certain of this by referring to figure 42. This figure was drawn by hand. Therefore the word "nystagmus" is in quotation marks. If we compare "nystagmi" a, b, c, and others, the difference among them raises no doubt: "nystagmus a" as compared with "nystagmus b" has a lower frequency and it reflects a certain drift toward FC. In "nystagmus c" impulses differ drastically in terms of duration, i.e. frequency is unstable. In the case of "nystagmus e", drift is toward SC, etc. In addition, all these "nystagmi" exhibit a definite similarity if the artificial technique described is used to eliminate the effects of the FC system and to determine the activity of the SC system. All five "nystagmi" produce the same CC graph, since differences among them were due only to features of the activity of the FC system. Using this characteristic makes it possible to very clearly determine the similarity of reactions when their differences are due, by their very origin, to the different levels of involvement of the SC system.

Using the characteristic described can be especially helpful when a complex nystagmic reaction is being analyzed, since elimination of any nystagmus features which owe their origin to the fast component system makes it possible to clearly represent processes going on in the slow component system and to stress indicators valuable in the diagnostic sense.

Multidimensional Characteristics and a Definitive Diagnostic Rule

In many cases individual ENG's can be differentiated from the norm by comparison with the norm in terms of any one characteristic. If this characteristic is one of the normally distributed (e.g. $\overline{F}$) characteristics, then it is simply compared to the arithmetic mean for the sample of identical functionals for the norm. This comparison makes it possible to solve the problem of differentiating with regard for variability of the norm, i.e. a discrepancy is considered certain if the difference exceeds twice the root-mean-square deviation. If lognormal characteristic distribution is used (e.g. $\overline{\omega}_{SC}$), the logarithm of the characteristic should be compared to the sample of logarithms for like characteristics, i.e. the approach remains, in principle, unchanged. It is more difficult to identify a pathology when individual characteristics do not exceed the statistical boundaries of the norm, but only the relationships between them are disturbed. Plotting mutual distribution of characteristics, i.e. the statistical distribution of the norm in which relationships between different characteristics are accounted for, may be used as a special technique for these

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problems.

T_R, $\bar{\omega}_{SC}$, and $\bar{F}$ were selected to plot mutual distribution [129, 412]. With this set, it could be asserted that features of both (tonic and rhythmic) systems which form nystagmus, as well as features related to the shape and intensity of the reaction, would be accounted for in a generalized three-dimensional characteristic. As a test showed, mutual distribution of the sample for F and the two samples for natural logarithms -- T_R^L and $\bar{\omega}_{SC}^L$ can be regarded as a three-dimensional normal distribution. (Similarly, mutual distributions can be plotted for other sets of characteristics, e.g. T_R^L, $\bar{\omega}_{SCint}^L$, F_{int}).

Further, a formula was found to calculate d_1, which represents a measure of the difference (square form of the deviation of sample parameter values from corresponding averages, which, for simplicity, we will call distance) of an individual nystagmic reaction from the average normal reaction. The magnitude of the distance can be used to judge the probability, in the norm, of a reaction with precisely these relationships among characteristics, as in the individual reaction of a specific subject which was studied. In other words, d_1 can be used for diagnostic purposes.

Let us introduce the equation for calculating d_1:

$$d_1(T_R^L, \bar{\omega}_{SC}^L, \bar{F}) = 10.34\Delta_1^2 + 4.72\Delta_2^2 +$$

$$+ 7.77\Delta_3^2 + 0.28\Delta_1\Delta_3 - 0.23\Delta_1\Delta_2 - 4.94\Delta_2\Delta_3,$$

where Δ_1, Δ_2, Δ_3 are deviations from corresponding arithmetic means for characteristics on a specific ENG studied for diagnostic purposes for a group of healthy (cf. table 14) humans, while coefficients are found for the sample of normal ENG's. Subscript "1" for a given d is used to identify type 1 diagnosis, in contrast to type 2, which identifies type 2 diagnosis (cf. below). The problem-solving rule (the decisive diagnostic rule) for the difference between the sample value and that permissible in the norm (given a 5% level of significance) is formulated as: if $d \geq \chi^2_{n(0.05)}$, i.e. $1-p(\chi^2 \leq d) \leq 0.05$, then the case can be assigned to the category of those differing from the norm and the probabiltiy of error in this solution will be less than 5%. A condition for statistically classifying an ENG as pathological when this equation is used is that $d_1 \geq 7.82$, since $\chi^2_{n(0.05)} = 7.82$ [25].

Table 16 shows use of type 1 diagnosis in a specific example. This example is of interest because, first, the injured side is definitely known and, second, not one single characteristic in either of the two ENG's (results of two cool tests) exceeded the limits of the 95% confidence range when compared with like characteristics, i.e. it was not possible to /145

identify the pathology with the traditional approach. Diagnosis based on mutual three-dimensional distribution made it possible to determine that the ENG obtained during a test on a healthy ear differed from the norm.

TABLE 16. EXAMPLE OF THE USE OF TYPE 1 DIAGNOSIS (d_1) TO EVALUATE TWO ENG's RECORDED IN ONE PATIENT (CLINICAL DIAGNOSIS: CHRONIC SUPPURATIVE MESOTYMPANITIS ON THE RIGHT SIDE [129])

Test	DR			SSC			Frequency		
	T_R, sec	T_R^L	Δ_1	$\dot{S}C$, sec^{-1}	$\bar{\omega}_{SC}^L$	Δ_2	F, sec^{-1}	Δ_2	d_1
Cool test from left	110	4.70	-0.57	6.93	1.93	-0.89	1.19	-0.75	8.22
Cool test from right	116	4.75	-0.42	8.87	2.18	-0.64	1.31	-0.68	5.84

NOTES: 1. Deviations Δ_1 and Δ_2 were calculated not from initial ENG characteristics, but from their logarithms. 2. Deviations in individual characteristic values were calculated using averages for the set of norms in table 14: $\Delta_1 = T_R^L - 5.27$, $\Delta_2 = \bar{\omega}_{SC}^L - 28.2$, $\Delta_3 = \bar{F} - 1.94$. 3. Conclusion: Nystagmus produced in the test on the left reliably differed from the norm ($d_1 > 7.82$, $P < 0.05$).

According to the table for the probability integral χ^2 [25], it can be determined that, once an ENG recorded during a test on the left (healthy) ear is taken to be pathological, the error in judgment is assumed to be only 4%. The second ENG is not pathological, since the error in making this conclusion would be too great (12%). This example shows that a type 1 diagnosis actually facilitates observation of vague deviations from the norm. In addition, it must be stressed that it can be used only for formal determination of the existence of a deviation, but other conclusions (e.g. on which side is injured, injury level, mechanisms, etc.) cannot be made. In this example the pathological reaction was observed upon stimulation of the healthy ear. These results apparently stem from the fact that, during any stimulation of one labyrinth, nystagmus is the result of interaction of a pair -- the right vestibular apparatus with the corresponding vestibular nuclei and the left vestibular apparatus with its nuclei (cf. chapter 4).

The primary difference in type 2 diagnosis is that the relationship among reactions caused by stimulation of the right and left labyrinths, i.e. the existence in the norm of certain relationships within a pair of reactions, accounted for [129].

In the norm, a positive correlation of T_R^L's during right- and left-side tests has been observed. Relationships similar in nature exist between ω_{SC}^L's and F's. Figure 40 shows examples of these correlation fields. It is natural to assume that, given certain pathological conditions in the vestibular function, the nature of these relationship may vary and that this change may be a useful diagnostic indicator suitable for differentiating a pathology from the norm. Type 2 diagnosis should answer the question whether a pair of reactions recorded in a given subject differs in terms of a single symptom from those which occur normally: the nature of the relationship between like characteristics in nystagmi produced during right- and left-side tests. It should also determine the probability of error in evaluating the difference. /146

A simple way to test the success of type 2 diagnosis was selected: plotting two-dimensional distributions of like characteristics. Three distributions were plotted: 1) from T_{Rr} and T_{Rl}, 2) from ω_{SCr} and ω_{SCl}, 3) from F_r and F_l. The following are the equations used to calculate $d_2(X)$ in terms of each of the three distributions:

$$1)\ d_2(T_R^L) = 37.2\Delta_r^2 + 38.87\Delta_l^2 - 65.60\Delta_r\Delta_l.$$

where $\Delta_r = T_{Rr}^L - 5.24$, and $\Delta_l = T_{Rl}^L - 5.29$;

$$2)\ d_2(\bar{\omega}_{SC}^L) = 7.46\Delta_r^2 + 5.13\Delta_l^2 - 7.39\Delta_r\Delta_l,$$

where $\Delta_r = \bar{\omega}_{SCr}^L - 2.76$, and $\Delta_l = \bar{\omega}_{SCl}^L - 2.87$;

$$2)\ d_2(\bar{F}) = 9.39\Delta_r^2 + 9.00\Delta_l^2 - 10.76\Delta_r\Delta_l,$$

where $\Delta_r = \bar{F}_r - 1.97$, and $\Delta_l = \bar{F}_l - 1.92$;

Table 17 shows the example of using type 2 diagnosis as compared to the results of type 1 diagnosis. In this example, a pair of nystagmi was evaluated three times and it was sufficient that a deviation from the norm be discovered during comparison of even one of the two-dimensional distributions. In all cases, $d_2 \geq 5.99$ was taken as an indication of deviation from the norm (given a 95% confidence range); d_2 is the square form of deviations from averages obtained individually for two ENG samples, i.e. for right- and left-side tests.

This example of using type 2 diagnosis is indicative, as was the previous example, in that values for individual quantitative characteristics of nystagmic reactions did not exceed the limits of the 95% confidence range, i.e. it was also impossible to identify a pathology by traditional means. During testing with type 1 diagnosis (i.e. using mutual three-dimensional distribution) it was also impossible to obtain indications of a deviation from the norm (probability of error for each individual ENG was about 50%). Only type 2 diagnosis /147

revealed a discrepancy between an ENG and the norm; this discrepancy was observed only in terms of one characteristic (T_R).

TABLE 17. EXAMPLE OF USING TYPE 2 DIAGNOSIS (d_2) TO EVALUATE TWO ENG's RECORDED DURING COOL TESTS ON ONE PATIENT (CLINICAL DIAGNOSIS: MENIER's DISEASE IN REMISSION) AND THE RESULTS OF EVALUATING THE SAME ENG'S BY TYPE 1 DIAGNOSIS (d_1)

Type 2 Diagnosis (Deviation from Norm with $d_2 \geq 5.99$)			Type 1 Diagnosis Deviation from Norm with $d_1 \geq 7.82$)	
In terms of			Right Test	Left Test
T_R^I	ω_{SC}^I	F		
$d_2=19.48$	$d_2=0.30$	$d_2=1.99$	$d_1=2.53$	$d_1=2.66$
$p < 1\%$	$p = 86$	$p = 37$	$p = 49$	$p = 46$

NOTES: 1. p -- probability of error in defining the subject pair of ENG's (for d_2) or an individual ENG (for d_1) as deviating from the norm. 2. Conclusion: The subject pair of ENG's reliably deviates from the norm in terms of the relationship between T_R^I's ($d_2 = 19.48$, $P < 0.01$).

The significance of generalized (multidimensional) nystagmometric characteristics in applied nystagmometry is obvious. First, they are suitable for professional examinations, when only establishment of the fact that a deviation from the norm exists, not a statement of diagnosis, is required. The time required to process material is not a major drawback, since the result can be obtained automatically [130]. Second, use of these techniques in the clinic demonstrates their effectiveness in defining the dynamics of a pathological process (e.g. in the post-operative period during stapedioplasty, d_1, gradually decreasing to 7.83 or less, can be considered an indication that the condition of the vestibular system is normalizing). It is entirely possible that these techniques will be useful for evaluating the effectiveness of several rehabilitative measures, in vestibular training, as a means to overcome motion sickness, and also to test drugs for ototoxicity. In one study, a procedure for generalized nystagmometric evaluation was refined and applied to rotatory tests [43]. On the one hand, a correlation between deviations in distance (i.e. in terms of d_10) was discovered; on the other hand, the level of vestibulo-vegetative instability was defined. This presents opportunities for applying multidimensional characteristics to identifying a group of risks during professional screening for several specializations

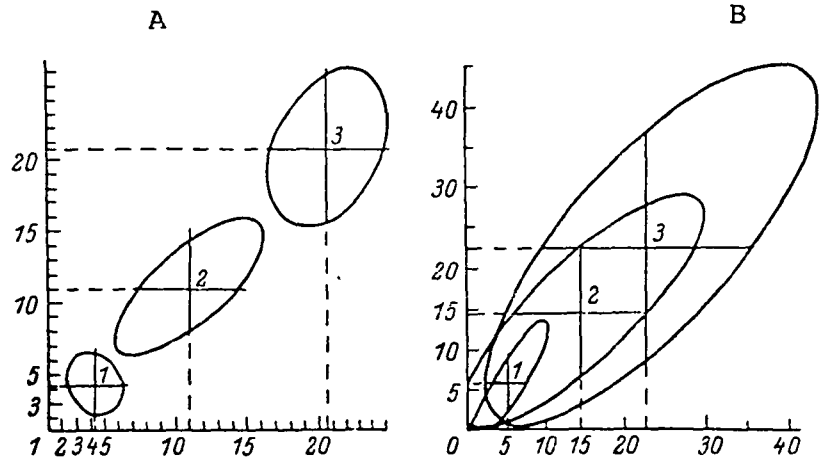

Figure 43. Optokinetic nystagmus. Generalized nystagmometric characteristics demonstrating the principle of type 2 diagnosis (from [138].

X-axis: A -- Average SSC of rightward OKN in a 20-sec segment of an ENG, $^{\circ}\cdot sec^{-1}$; B -- Frequency of rightward OKN (number of nystagmic impulses in the same ENG fragment); Y-axis: corresponding like characteristics of leftward OKN. The scope of each sample: 39 pairs of like OKN characteristics. Straight lines show coordinates of mathematical expectation in two-dimensional distributions obtained at three OKS speeds: $4^{\circ}\cdot sec^{-1}$ (1); $10^{\circ}\cdot sec^{-1}$ (2); and $20^{\circ}\cdot sec^{-1}$. Ovals designate the zone of the 95% confidence level for each two-dimensional distribution.

connected with the effect of factors harmful to the vestibular system, especially in aviation and aerospace, in high-speed land transportation, et al.

Let us present one more example of a successful attempt to expand the scope of application of multidimensional characteristics. In a study of optokinetic reactions in the norm [138], two-dimensional characteristics were plotted for type 2 diagnostic purposes. Mutual distribution was plotted and coefficients for distance equations were found for each of six samples (OKN SSC and frequency from three OKS's). The boundaries of the 95% confidence range for each sample are shown graphically (cf. figure 43). The obvious difference in terms of SSC and frequency boundaries is clear. In terms of frequency, a significant positive correlation between right- and leftward reactions was observed at all three OKS speeds. In contrast to frequency, evaluation of the SSC shows a strong correlation only with a stimulus at $10^{\circ}\cdot sec^{-1}$; there was none at $4^{\circ}\cdot sec^{-1}$. In other words, OKS speed is reflected differently in correlations of characteristics belonging to OKN tonic and rhythmic systems.

The equation for calculating square deviation of distance d_2 for a two-dimensional distribution has the same form as that above (if caloric nystagmus is being evaluated), but is distinguished only by its coefficients:

$$d_2 = a\Delta_1^2 + b\Delta_1\Delta_2 + c\Delta_2^3,$$

where Δ_1 is the difference between the value of the subject characteristic in a rightward OKN in a test subject and the corresponding mathematical expectation (i.e. $\bar{x}$ in table 8); Δ_2 is the same for leftward OKN in the same test subject at the same stimulus speed (in this case $\bar{y}$ in table 8 should be used); a, b, and c are coefficients introduced in that table for each of the six samples. Coefficients were obtained by transforming original paired samples applied to type 2 diagnostic problems. /149

Several simple calculations are required to determine whether a pair of optokinetic reactions in a subject deviates from the norm in terms of the relationship between OKN characteristics. First, average SSC (e.g. for a 20-sec recording segment) must be calculated for each of the two OKN ENG's recorded for the subject at one OKS speed. Second, Δ_1 and Δ_2 are calculated as the difference between the values obtained from processing the ENG's and the corresponding mathematical expectation in the norm. Third, appropriate coefficients (a, b, c from table 12) should be substituted into the equation for calculating d_2 and the distance determined. If $d_2 \geq 6.0$, relationships between characteristics in a pair of OKN's can be considered to deviate from the norm (error is less than 5%). The significance of the error can be defined from the probability integral table, just as in caloric tests. If there is no need to know the precise numerical value of d_2, a graph of the type shown in figure 44 can be used. When the point at which the horizontal coordinate (characteristic of rightward nystagmus) intersects with the vertical (leftward) is found, the diagnostic solution is found depending on whether this point lies inside or outside the outlined area of the 95% confidence level. In all cases when the point is outside the zone, the subject pair of OKN's is considered to deviate reliably ($P < 0.05$) from the norm. Graphs are convenient for large-scale investigations, since calculations with the equation can be avoided.

Graphs (cf. figure 43) make it possible to visually ensure that OKS speed is actually relevant in studies of the optokinetic system. In particular, the dimensions of physiological asymmetry are a function of stimulus speed. Let us find the point at which coordinates $x(OKN_r)$ and $y(OKN_l)$, which are sufficiently different, intersect in each of the three zones (cf. figure 43), i.e. let us represent an imaginary pair of OKN's lying within the limits of the norm but, at the same time, noticeably asymmetric in terms of SSC. We will present the results in the following form:

Stimulus °·sec^{-1}	x °·sec^{-1}	y °·sec^{-1}	Difference in SSC's	
			Absolute °·sec^{-1}	Relative %
4	2.5	5.0	-2.5	-33
10	5.5	7.5	-2.0	-15
20	16.5	19	-2.5	-7.3

It is obvious that relative asymmetry decreases insofar as /150
there is a transition from low stimulus speed to a higher speed, i.e. each distribution has its maximum permissible level of relative physiological asymmetry in terms of SSC.

This is not the case with frequency: for example, a point with coordinates x = 3.0 and y = 5.5 belongs equally to all three distributions. Relative asymmetry in this pair is -20%, i.e. the considerable relative asymmetry in terms of frequency is quite normal for OKN's caused by any of the three stimuli. The variability in distributions plotted for OKN frequency is greater than that for SSC frequency. Therefore, all three zones of 95% confidence are superimposed on one another. Keep in mind that the material considered here, first, applies to OKN's in children and, second, was obtained with a nontraditional figure projected on the screen [138], i.e. frequency was entirely independent, for example, of the number of bands in the field of vision, their angular dimensions, duty factor, and other factors. However, despite this last remark, it is apparently always necessary take a careful approach to diagnostic research in which conclusions are based only on the results of evaluating OKN frequency; it is an obvious conclusion that comprehensive evaluation of nystagmus with regard to the properties of reactions caused both by rhythmic and by tonic system are required [118].

The principles of type 2 diagnostics (cf. figure 43) were used to evaluate the results of the modulating effect of vestibular stimulation on OKN's [139]. Chapter 2 discusses the

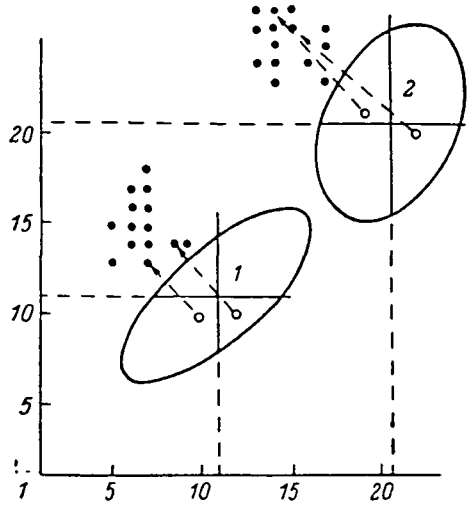

Figure 44. Modulation of OKN exposed to stimulation of the vestibular apparatus. Evaluation of the effect of modulation according to type 2 diagnostics.

X-axis -- Average SSC in a 20-sec ENG segment of a rightward OKN, $^{\circ}\cdot sec^{-1}$; Y-axis -- same for leftward OKN. Ovals -- zones of 95% confidence for two-dimensional distribution in the norm (as in figure 43) for two OKS's: (1) $10^{\circ}\cdot sec^{-1}$ and (2) $20^{\circ}\cdot sec^{-1}$. Solid dots correspond to individual two-dimensional characteristics obtained for pairs of OKN's modulated by cool stimulation of the right labyrinth. Dotted lines with arrows show examples of shift in original characteristics (hollow dots) beyond the limits of the norm zone upon additional vestibular stimulation.

effect itself in detail. Figure 44 shows that all modulated reactions lay outside the limits of the 95% confidence range. In other words, in each pair of reactions (VOKNC-VOKNN), asymmetry was statistically reliable. This figure shows trajectories of shifts in two-dimensional characteristics beyond the limits of the norm are several pairs. /151

The large number of nystagmometric characteristics considered in this chapter results from an attempt to statistically study the largest possible set -- without claiming, of course, that it is an exhaustive list of all possible characteristics. From this set the experimenter, guided by specific research goals, can select the characteristics most important from his own point of view.

Determination of the type of characteristic distributions, especially detection of a large group of lognormal distributions should promote a more justified use of Student's criterion, which is quite widely used in biological research.

The attempt to systematize nystagmometric characteristics

to show their meaning, their use in applied work, and their information value, will apparently encourage acquisition of comparable results in experiments conducted by various procedures and on various subjects.

Reviewing the relationships between nystagmometric characteristics and, especially and establishing two classes known to be autonomous give rise to new problems in theoretical nystagmometry in terms of future research on the mechanisms of nystagmus (including adaptation, adjustment, and compensation), as well as for applied nystagmometry, since it can be important in diagnostic research to account for deviations from the norm in characteristics which represent different classes.

Chapter 4. A Diagnostic Model of a Bithermal Test /152

The anatomical-physiological features of the labyrinth, with the three-dimensional receptor formations of its semicircular canals and vestibula, the hydromechanical processes in the cupuloendolymphatic system as primary factors in the functioning of this biological accelerometer, the proportionality and paired strucure of head version speed afferentation, the vectorial nature of vestibulosomatic reflexes, the ability to record and quantify these reflexes -- these and certain other features make the vestibular system and its reaction an interesting object for modeling: physically, electronically, and mathematically [4, 14, 36, 49, 163-165, 199, 346, 419, 455, 484, 521].

In medicine, mathematical models have limited application because the accuracy of results depends on correct identification of appropriate parameters, on the accuracy and determinateness of the relationships among them, and on the accuracy of methods used to measure them [209].

It is understood that the field of nystagmometric diagnostics is one where it is entirely possible to quantify processes, where definite relationships among parameters are, to a significant extent, defined, and where the measuring accuracy achieved is adequate, i.e. there are conditions favorable for creating a mathematical model for diagnostic purposes.

If a classification providing for three types of models -- physical, material-mathematical, and logical-mathematical [28] is used, then the model discussed in detail below, which we have proposed [123], should be classified in the latter category, since it has the qualities of models of this type: it is based on signs and its description is inseparable from the model itself.

Statement of the Problem. Purpose of the Model

The set of caloric tests consisting of warm and cool tests on each ear [263, 210, 351, 502] is quite important in vestibular practice. This set, called the bithermal test (BT), constitutes the required minimum without which objective quantitative evaluation of the condition of the vestibular function is hardly possible. BT results are used to obtain the coefficients required for diagnosis: labyrinth asymmetry (K_{LA}), directional preponderance (K_{DP}), and rarely, thermostimulus effectiveness (K_{TE}). Note that only the term "directional preponderance" (DP) can be considered to have been generally accepted [230, 263, 310, 341]. It is used to identify the prevalance of nystagmus in terms of direction, i.e. the measure of the difference between reactions in opposite directions. The term "labyrinth asymmetry" (LA) used in this monograph in the same sense as the terms "unilateral weakness" [268], "vesti- /153

bular paresis" [230], and several others are used, is more suitable because it denotes a measure of the difference in labyrinths in terms of reactivity, which may result not only due to a decrease in reactivity, but also due to an increase. K_{TE}, reflecting the difference in reactions to heat and cold, has not been widely used in practice, but is necessary for the model under consideration.

K_{LA} and K_{DP} must be produced if the BT is to have logical completeness. Figure 45 shows the system for evaluating the results of BT. Results obtained as a result of BT's are conveniently generalized in a table and presented in the form of a diagram [247]. For K_{LA} the result with a plus sign means that the right labyrinth predominates in terms of reactivity, while for K_{DP} a plus denotes the predominance of rightward nystagmus. Note that the sequence for calculating the difference is not strictly regulated and that literature provides another technique, where K_{LA} is calculated by taking ENG characteristics obtained in tests on the left ear as those to be decreased, while those to be subtracted are obtained from tests on the right ear. The approach for calculating K_{DP} is similar in these cases. Normally, all three coefficients may differ from zero. There are limits within which the fact that coefficients differ from zero is not considered a sign of pathology. Literature provides information on the physiological limits of variations in these coefficients [230, 268, 383, 506, 570]. Formally, any total characteristic can be used to calculate coefficients. The most valuable information comes from characteristics in the intensity class (e.g. in terms of culmination SSC). The limits of deviation from zero levels for K_{LA} and K_{DP} are somewhat different: according to data from various authors, K_{DP} varies much more. Variations permissible in the norm, measured as twice the standard deviation for K_{LA} and K_{DP} (in terms of SSC), constitute about $\pm$20% [268].

K_{LA} and K_{DP} are not of equal diagnostic significance. Each can be considered reliable evidence of the existence of vestibular dysfuntion, but relative localization of the pathological process can be assessed only in terms of one of them -- K_{LA}. A deviation in K_{LA} beyond the permissible /155
indicates peripheral pathology, i.e. disturbances occurring in the labyrinth itself or in the vestibular nerve trunk. K_{DP} can go far beyond the limits of the norm both in peripheral and in central localization of the pathological center [230, 268, 506]. Calculating K_{DP} does not facilitate topical diagnosis. According to Hallpike's (one of the authors of BT) prototype equation [342], "directional preponderance can cause false hopes and misunderstanding" for those who use BT for diagnostic purposes.

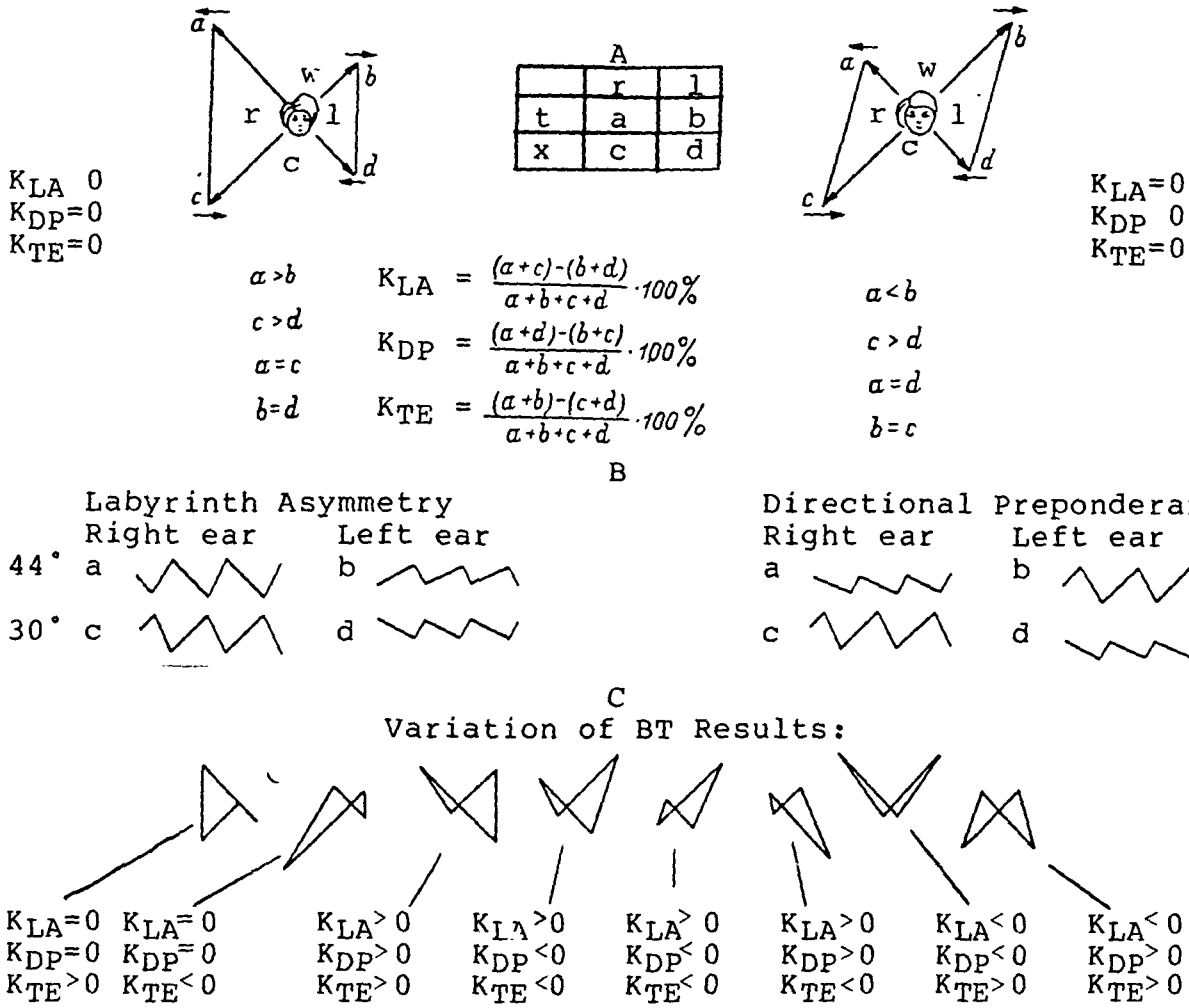

Figure 45. Diagram for evaluating a bithermal test and certain alternative results of this test, observed in diagnostic practice.

A -- Intensities obtained in BT on four nystagmi (a, b, c, and d)) caused by various warm (m) and cool (x) stimuli from right (r) and left (l), imposed on axes of two corresponding vector diagrams. Horizontal arrows on the diagrams show the direction of caloric nystagmi in each test. Equations for calculating diagnostic coefficients -- labyrinth asymmetry (K_{LA}), directional preponderance (K_{DP}) and thermostimulation efficiency (K_{TE}). B -- Fragments of conventional nystagmograms demonstrating examples of two extreme variations "pure" LA and "pure" DP. If these two variations are similar in terms of relationships between cool nystagmi, there is a basic difference in vestibular dysfunction mechanisms which can be observed only if information is available on thermal nystagmi. C -- Certain examples of diagrams and corresponding relationships between diagnostic coefficients -- from those occurring in practice.

The diversity of other K_{LA} and K_{DP} combinations is rather great. Figure 45 shows examples of diagrams of the results of BT occurring in the practice of diagnostic research.

As regards conditions under which a specific BT result is produced, only individual observations are available. Thus, for example, there is information that DP rarely correlates with spontaneous nystagmus [401]. It is apparently more correct to state that, if spontaneous nystagmus is present, the probability of DP increases substantially. The sign of K_{DP} often corresponds to the direction of the spontaneous nystagmus, but this is not a rule. It is also possible both that signs will not match and that DP will exist without spontaneous nystagmus. Considerable difficulties arise in interpreting results when K_{LA} and K_{DP} signs differ. In other words, K_{LA} and K_{DP} values outside the norm are a reliable indication of pathology, but they are a formal sign, inadequate to determine the disturbing mechanisms in each specific case.

Therefore, it is useful to develop a model designed to eliminate extra information from BT results, i.e. for work in diagnosing vestibular dysfunction [123, 124]. By serving this basic purpose, the model can be used for experimental-theoretical research. The model can be used to predict results of experiments and gain an understanding of possible mechanisms of directional preponderance. The model has made it possible to give a competent explanation of the phenomenon of sign change in K_{DP}, observed during a study on nystagmus during a sinusoidal rotation test [126]. Finally, note that the model has yet another purpose -- didactic: the model helps clearly understand how changes in the receptor apparatus and nerves are reflected in BT results.

When the model is used for didactic purposes, it is intended to answer a question such as: If conditions are preset to correspond to a certain pathological state, what will the results of the BT be?

When the model is used for diagnosis, the object is to answer a different question: If, as a result of BT, a specific result is obtained, what deviations from the norm caused this result?

The Essence of the Model /156

The result of each caloric test is considered to be a summary of the interaction of energy levels (EL) of two vestibular nuclear complexes (NC), right and left. Caloric nystagmus in the model is the direct result of the difference in NC EL on the right and left, while nystagmus intensity is proportional to the difference between EL's.

A direct cause for the changes in EL balance between two

NC's is a stimulus which changes the level of activity of one of them. The second NC at this time is considered as untouched.[1] In addition to the external cause (stimulus), the EL balance of two NC's may be disturbed due to a pathology even before the BT. These changes develop slowly and are considered as background on which a BT which is altered as compared to the norm occurs.

At each moment, the EL of one NC is composed of two components -- a certain inherent activity (IA) and afferent flow (AF). Pathological changes can occur in IA, AF, or both components. The pathology remains unchanged over the course of the BT. It can be localized in a receptor apparatus, nerve, or NC. Changing the background or capacity to react to a stimulus, the pathology creates conditions in which relationships between nystagmi produced as a result of the BT change as compared with the norm. These are the general features of the model.

Assumptions and Argument

Some assumptions which underly the model naturally arise from facts which are well known in the physiology and pathophysiology of the vestibular function, while others should be considered as specific hypotheses based on comparison of experimental and clinical observations. All assumptions are set forth here in the form of 16 points. Points 1-13 relate to the essence of the model. Point 14 has, one might say, temporary significance, since the concept of the norm is later clarified. Point 15 reviews types of pathology which are the most important. Point 16 makes the assumption that a mechanism to compensate for vestibular dysfunction is possible.

1. Nystagmus is directed toward the system of vestibular nuclei, right or left (NC_r and NC_l), whose energy level predominates at a given moment.

2. The intensity of the experimental nystagmus may be expressed in units of SSC in the culmination reaction segment.

3. The intensity of the experimental nystagmus is due only /157
to the difference between NC_r and NC_l energy levels. Intensity is proportional to this difference, but for practical purposes is regarded as equal to it[2].

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1 In fact, certain changes apparently also occur in the NC on the unstimulated side. In particular, information is available that, during prolonged exposure to angular acceleration, changes occur in activity of type I neurons in the upper vestibular apparatus of an ape on the side on which all three semicircular canals were sealed [217].

2 A similar technique for equating caloric nystagmus intensity to the difference in tonus of two nuclear complexes is used in another model [513].

4. In the absence of stimulation of the peripheral receptor apparatus, the difference in EL levels of the right and left NC may differ from zero. In this case it can be regarded as small if there is no spontaneous nystagmus, or large, if spontaneous nystagmus occurs. In other words, a difference in EL is not necessarily associated with spontaneous nystagmus.

5. Experimental vestibular nystagmus occurring on the background of spontaneous vestibular nystagmus can be considered the result of addition with regard for the vectorial nature of background reactions and the effect of indirect stimulation.

6. The energy level (EL) of each NC at any moment consists of two components: inherent activity and afferent flow from the labyrinth along the nerve (cf. figure 46). In the absence of stimulation, AF equals the level of spontaneous impulsation (AF_{si}) and is stable. AF is measured above the SI level. If, for any reason (cf. point 15), AF equals zero, NC EL on this side cannot equal zero, since it retains a constant component -- SI.

7. SI level depends on the condition of neurons in a given NC and on the effect from the opposite NC. It is assumed that a noticeable contralateral effect requires long time segments. Therefore, this effect is felt in the reaction by virtue of the fact that NC is involved in formation of the background condition. During a BT, the background remains unchanged.

8. SI can change over considerable lengths of time, for example, by actuation of the mechanisms for compensating for vestibular disturbance. Since results of four caloric tests separated by relatively small time intervals are compared, SI levels are considered unchanged over the course of the entire BT. Each new BT conducted during study of the dynamics of the illness is considered a separate independent occurrence. NC's, already with a different SI level, may be involved in the formation of test results.

9. Original right and left SI levels may be identical or different -- their difference is not necessarily a sign of pathology.

10. The cupular apparatus is regarded as a single entity -- a sensor which reacts proportionally to the magnitude of cupuloendolymphatic shift and generates a certain average level of afferent flow in the vestibular nerve (i.e. the sum of the impulses passing through the cross section of the nerve over a unit of time). At every moment this AF corresponds to the position of the cupula -- the degree of deviation of the cupula /158 from neutral position.

11. AF moving along the vestibular nerve to an ipsilateral

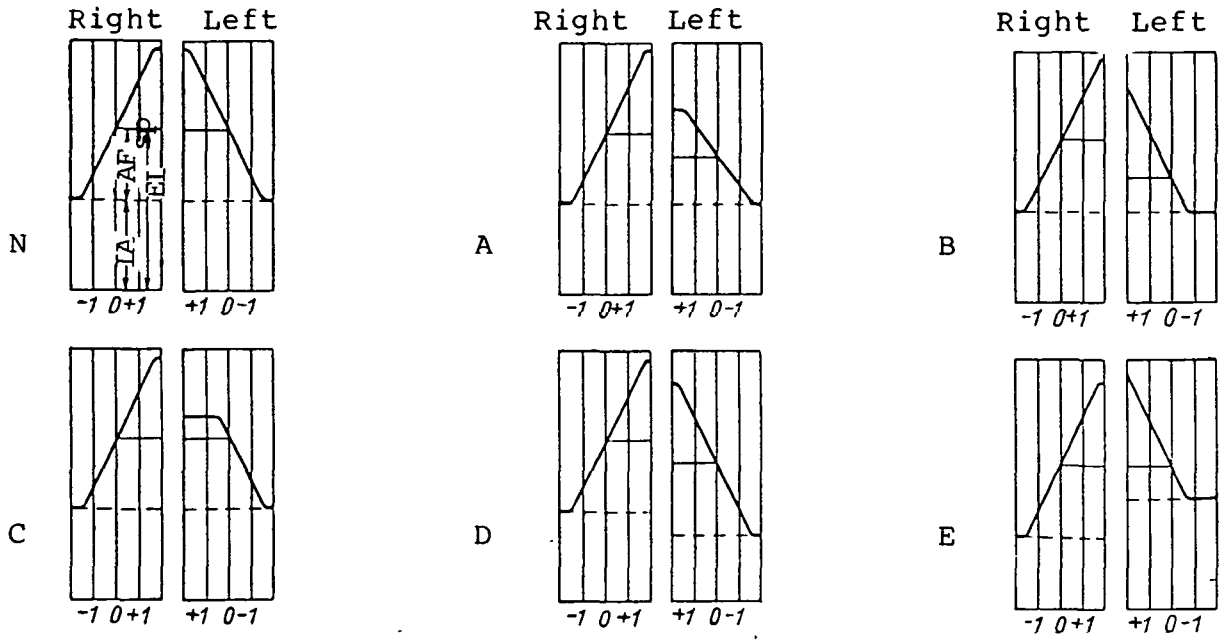

Figure 46. Model of BT in the norm (N) and during left-side pathology (A-E) (from [124]).

X-axis -- Cupuloendolymphatic displacement in response to warm (+1) and cool (-1) stimuli; Y-axis -- energy level (EL) of the corresponding (right or left) vestibular NC. EL (outside the stimulus designated by a solid horizontal line) consists of afferent flow (AF), shown as an S-shaped curve, and inherent NC activity (SI). *SI level is identified by the broken line.* AF outside the stimulus is equal to spontaneous afferent flow (AF_{sp}). Pathology variations: A -- Reduction in the slope in the AF characteristic; B -- Characteristic displacement; C -- Upper limit on characteristic; D -- Reduction in SI; E - Characteristic shift similar to that shown in B, but compensated by redistribution of SI.

NC is a function only of the position of the cupula of one semicircular canal, the one to which the caloric stimulus is directed. The entire AF travels only to the ipsilateral NC and, combining with SI, takes part in forming the EL of a given NC.

12. During a caloric test, the NC EL on the test side varies only due to changes in the AF traveling along the nerve from the semicircular canal exposed to the stimulation. If the nerve's conductivity is not disturbed, the scope and nature of the changes in NC EL completely correspond to changes in the receptor apparatus. The curve for AF as a function of the magnitude and direction of cupuloendolymphatic shift is S-shaped. The axis of the ordinates divides the AF characteristic into two unequal parts. The characteristics corresponding to the

utriculopetal deviation are about twice those corresponding to the utriculofugal. Outside the test, AF is stable and equal to the level of spontaneous activity (AF_{sp}). NC EL on the unstimulated side remains unchanged during the test. /159

13. The heating and cooling conditions used during the caloric test ($\pm 7^{\circ}C$) are associated in a healthy human with a cupuloendolymphatic shift whose afferent flow changes at the portion of the characteristic which is a straight line, i.e. changes occurring in AF are equal in magnitude and differ only in sign.

14. Full conformity of all right and left NC parameters is the norm: the equality of inherent activity levels and spontaneous afferent flows, an identical slope in the S-shaped characteristic, changes in afferent flow which are identical and symmetric for stimuli opposite in sign (cf. figure 46 N).

15. Pathology involves changes in a particular vestibular apparatus, vestibular nerve, and vestibular NC properties (separately or in combination). The types of changes are:

a) Type A pathology. A change in the characteristic's slope, i.e. AF as a function of the magnitude of cupuloendolymphatic shift. The slope may decrease (cf. figure 46 A) or increase.

b) Type B pathology is shown in figure 46 B. This is a characteristic shift along the horizontal when its normal steepness is retained.

c) An upper limit on the characteristic -- type C (cf. figure 46 C).

d) A change in the level of the constant NC EL component, i.e. its inherent activity -- type D (cf. figure 46, D). These changes may involve an increase or a decrease in SI.

16. The mechanism for compensating for vestibular dysfunction is activated when the EL's of two NC's become different and is intended to balance them. EL's are balanced because part of the SI is transfered from the dominating NC to the NC on the opposite side, as a result of which one EL diminishes while the other increases by the same amount (cf. figure 46 D). This mechanism occurs in types of pathology associated with a reduction in AF_{sp} level. Compensatory balancing of NC EL's proceeds rather slowly. Therefore, it can be stated that the results of a single BT depend on whether the compensation was completed by the time of the study. The difference in results of BT's when studies conducted over long time intervals are repeated may result from a different degree of compensation.

Below are the argument and certain comments on the assump-

tions underlying the model. NC should be understood to mean the totality of second-order neurons which take part in nystagmus development. Nystagmus intensity is evaluated in terms of culmination SSC, because SSC correlates with stimulus intensity to a greater extent than do other nystagmus parameters [350, 546, 555, 556]. The hypotheses in points 3 and 12 do not account for the role of contralateral effects, adaptation mechanisms, and efferent relationships, the study of which is in the initial stage. We now know only that these mechanisms exist [287, 303, 344, 438, 536]. There is still no information on how much and exactly how they are disturbed if there is a pathology. Therefore the model assumes that these influences act equally on all four BT nystagmic reactions. /160

The assumption that a difference between the EL's of two NC's exists without stimulation (point 4) is justified by observations, known from practice, of spontaneous nystagmus in humans who do not suffer from vestibular dysfunction, as well as by the fact that, in healthy humans, K_{DP} is not necessarily equal to zero. Experimental vestibular tests conducted on a background of labyrinthine nystagmus are accompanied by an intensified reaction if the labyrinthine nystagmus matches the spontaneous nystagmus in direction and by a weakened reaction if it does not (cf. point 5). The assumption that AP_{sp} is stable (point 5) is based on electrophysiological data: most units are characterized by regular spontaneous activity [305]. The classic research of V. M. Bekhterev [17] is evidence in favor of the existence of SI, i.e. a constituent which is not a direct function of AF, in NC. In particular, he studied nystagmi occurring during alternating disconnection of labyrinths starting on one side and then on the other. Spontaneous nystagmus after delabyrinthation was directed toward the side which previously lacked a labyrinth and was half as intense as spontaneous prolapse nystagmus after the first operation.

Consequently, an NC has a certain level of activity even without AF. The presence of NC SI is confirmed by other facts as well. For example, in dogs with bilateral statocoustic nerve dissection, additional damage to vestibular nuclei on one side caused several symptoms typical for unilateral disconnection of the vestibular apparatus, including nystagmus in the opposite direction [419].

A fact observed during experimental dissection of the vestibular nerve of a cat [442] indicates the possible significant reciprocal influence of NC's (points 7-8): second order neurons directly connected to the horizontal semicircular canal react to contralateral dissection by reducing electrical activity and sensitivity to acceleration.

The assumption made in point 9 and 16 regarding the compensation process is similar to familiar hypotheses originally postulated by Ruttin [526]. Compensation mechanisms have been

a subject of debate in literature for many years. As early as 1936, a manual published for physicians by S. M. Kompaneyts [89] contained information on experimental and clinical study of this /161
phenomenon and stated the hypothesis that it is based on a gradual increase in nuclear activity on the side of labyrinth function prolapse[1]. Remember that in V. M. Bekhterev's experiments [17], the second labyrinthectomy occurred after spontaneous prolapse nystagmus caused by the first operation had disappeared. In a study of VPN in rabbits lacking one labyrinth, a two-stage decrease was observed during compensation [46]. Restoring a stable balance in VPN in these animals required several (up to 6) months. Electrophysiological data was enlisted, and a model similar to that described was used to explain results in this study. In particular, restoration of post-rotatory reaction after unilateral labyrinthectomy was explained by the fact that activity is restored in the ipsilateral nuclei, primarily as a result of the effects of nuclei on the untreated side. Finally, there is information that, in cats, the intensity of reactions to rotation, evaluated in terms of SSC, decreases by half after unilateral labyrinthectomy [372].

Point 10 ignores the difference in types of ampullar receptors and first order neurons [588], well known in experimental physiology. This can be justified in part by the fact the receptors, spontaneously active and reacting linearly to cupulo-endolymphatic shifts, represent the bulk of the ampullar device [322].

AF behavior deserves more detailed treatment. After experiments on the isolated labyrinth of a fish [430, 431, 433, 434], it became obvious that different levels of activity (i.e. states of rest, excitement, and inhibition) are distinguished by the number of afferent impulses per unit of time. Similar changes in AF have been observed in various animals: frogs [420], cats [220], guinea pigs [563], rabbits [485], and apes [307, 328-330]. There is a rather detailed description of the behavior of afferent flow [503]. Electrophysiological studies have revealed two vital features. First, most spontaneously active units respond symmetrically at low stimulus intensity, i.e. by changing activity to an identical extent in response to inhibiting and exciting actions. Second, high-intensity stimuli can, given an exciting effect, cause activity saturation and, given an inhibiting effect, cause complete disappearance of impulsation (silence). It has been noted that silence occurs when the inhibiting effect is smaller in absolute value than the stimulus which causes saturation. In other words, the AF characteristic is limited from above and below and there is a linear segment between them, while the level of spontaneous activity lying /162
within this segment divides the characteristic into two unequal

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1 The opinion exists that compensating mechanisms come about only at the level of cortical centers during asymmetry [95].

parts, wherein the length of the upper part is about twice that of the lower. Thus the approximation of AF using an S-shaped curve (point 12) can be considered to correlate with electrophysiological data [332, 561, 562]. AF as a function of the magnitude of the deviating cupulus of a stimulus which is S-shaped explains the well known and, as it has turned out, quite successful analogy with the characteristic of a triode, whose anodic current is controlled by net potential [332]. This analogy has been reinforced in several studies (especially [169]). We know that the signal to the vestibular nuclei consists of a change in impulsation in primary neurons proportional to head version speed and that this signal is replicated by many second-order neurons [455, 457]. The similarity in the dynamics of second-order neuron (i.e. NC component) activity to the activity of first-order neurons (i.e. afferents) is conclusively demonstrated, for example, in electrophysiological experiments on cats [222]. Approximation of nuclear neuron activity using an S-shaped curve completely coinciding with the characteristics for activity in the nerve was, in particular, successfully used to explain certain facts observed during rotatory tests in unilaterally delabyrinthated rabbits [46].

The proposed model uses a similar approximation, but it relates only to that portion of NC activity which is connected with AF, just as the entire EL is formulated in the form of the sum of AF and SI. This divergence from preceding models is quite significant, since it makes it possible to represent mechanisms for compensating for vestibular asymmetry in the form of a simple mechanism for balancing the EL's of two NC's by exchange of a portion of SI between them. In addition, the assumption that SI exists to a certain extent independently of AF makes it possible to consider several pathological conditions as having central genesis. Finally, it is precisely this assumption which has permitted solution of several problems related to the origin of DP.

The fundamental result of a discussion of Ewald's second law was, as we know, the following conclusion: the law is valid for high-intensity stimuli and unsuitable for minor stimuli. The category in which stimuli used in BT's are classified determines the competence of the assumption, made in point 13, that warm and cool nystagmic reactions are symmetric. Literature offers information about nystagmus caused by angular acceleration after separation of one labyrinth or nerve [217, 231]. It shows in particular that asymmetry of reactions to positive and negative acceleration becomes noticeable only at stimulus magnitudes capable of causing nystagmus with an SSC of at least $60^{\circ}\cdot sec^{-1}$ [231]. Since, during a gradual increase in the minus stimulus, the silence zone is reached sooner than /163
is the saturation zone in response to the plus stimulus, the appearance of asymmetric responses in this study should be attributed precisely to the silence zone. Consequently, if, during a cool caloric test, SSC is normally substantially less

than $60^{\circ} \cdot sec^{-1}$, it can be stated that the stimulus chosen causes AF changes only within the limits of the characteristic section which is a straight line. A traditional BT guarantees these conditions. This is evidenced by data obtained during a study of nystagmometric characteristics of cool reactions during a gradual increase in the level of labyrinth cooling [558]. It is also evidenced by data from statistical evaluation of SSC during cool tests [129], as well as the results of research on model parameters in the norm [129] which indicate the absence of a definite quantitative difference between the effects of warm and cool stimulations of different magnitude. We might add that there is information on the linear increase in maximum SSC during cool stimulation at temperatures up to +20°C [325] and even up to +17°C, i.e. to a level 20°C different from body temperature (from [582]). Since AF normally changes only in the straight segment of the characteristic during BT's, we can avoid precise reproduction of the S-shape curve during practical application of the model, make the two halves of the graph identical, and only nominally designate the horizontal segments of the characteristics beyond the limits of the stimuli as ± 1.

The hypothesis that all parameters for the two NC's are normally completely symmetrical is required only during initial familiarization with the mode and when the model is used for dynamic purposes. This hypothesis should be repudiated when solving diagnostic problems, and one should be guided by the range of variations inherent to the norm.

Of course, there is no direct experimental data relative to the variations in pathology assumed in the model (point 15). However certain comments are possible and necessary.

Oppression of receptors (type A pathology, cf. point 15 a and figure 46 A) is accompanied by a decrease in AF_{sp} and, consequently, by a decrease in the EL of the corresponding NC outside stimulation. The change in AF in response to a standard stimulus is, in this case, less than that in the norm. This deviation from the norm is, apparently, most often the case. But we must also assume a diametrically opposite alternative -- an increase in the characteristic's slope due to the excited state of the receptor apparatus. AF_{sp} level increases and NC EL rises correspondingly, while changes in AF in response to stimulation will be greater.

Characteristic shift along the horizontal (type B pathology, cf. point 15 b and figure 45 B) is associated with a reduction in AF_{sp} and, correspondingly, a decrease in the EL of the ipsilateral NC. If the shift is small, i.e. if the stimulus acts as before on the receptor only within the limits of the straight portion of its characteristic, then everything is /164
limited only by a certain NC EL reduction. If the shift is great, then, upon negative stimulation (i.e. during utriculo-

fugal cupuloendolymphatic shifts) the nystagmic response will not be a linear function of stimulus magnitude. The response to a standard negative (cool) stimulus turns out to be less than that for a positive stimulus. Formally, this type of pathology can be considered as a lower limit on the S-shaped characteristic.

Given type C pathology (point 15 c and figure 45 C) the effect of the positive stimulus can be less than that of the negative, since the saturation segment of the S-curve is reflected in nystagmus intensity if the segment lies within the limits of action of the standard stimulus.

Type D changes (point 15 d and figure 46 D) are accompanied by a corresponding change (decrease, increase) in NC EL on the ailing side.

These four types of pathology covered in the model may exist both independently and in various combinations on one side. They can occur due to various functional or morphological distubances.

How justified are assumptions made relative to the various forms of nystagmus?

The graph of AF as a function of stimulus, i.e. the S-shaped curve, is, as noted, a generalized slope connecting the properties of various elements which are incorporated into it as components. It is quite natural that the prolapse of any component be reflected in the characteristic's shape. If we imagine that element properties correlate with their morphology and that morphology, in turn, is related to an element's topography, then local injury must be accompanied by fundamental distortion of particular functional qualities. Let us refer to literary sources.

Electrophysiological research tells us that individual structures of the receptor apparatus of the horizontal canal ampulla are functionally heterogenous [528]. This heterogeneity amounts to differences in the level of activity at rest, a difference in the regularity of this activity, a difference in sensitivity to a stimulus, and a capacity for adaptation. On the basis of a study of features of spontaneous activity of first-order afferents in the lateral canal of a cat, for example, three groups of units were identified: regular, irregular, and intermediate [588]. A regular unit (i.e. one whose spontaneous activity is characterized by the smallest variational factor) is characterized by a high frequency of spontaneous activity and a low sensitivity to angular acceleration, not usually by adaptation. Irregular afferents are characterized by low frequency of activity at rest, high sensitivity to angular acceleration, and a tendency to adaptation upon prolonged exposure to stimulation.

The functional features of primary afferents (especially /165
their sensitivity to angular acceleration), correlate with morphological features. The little data available is, therefore, especially valuable. Isolated clivus labyrinth preparations in an electrophysiological experiment using cross-correlational statistical techniques and a special stimulus ("white noise"-type angular acceleration) showed that afferent sensitivity to acceleration correlates with internal crist topography, i.e. with these structures localized on it, as well as with vestibular nerve fiber arrangement and thickness [482]. Structures located in the central part of the crist, in contrast to those localized on the periphery, are most sensitive and, at the same time, tend to adapt.

Information is available that cats' primary vestibular afferents, in which spontaneous activity is regular, occur most often in that part of the vestibular nerve where thin fibers predominate, just as irregular activity is more typical of large-diameter axons [579].

Relying on these facts, we can hypothesize that, given the action of a particular harmful factor on afferents which differ morphologically, one of them is capable of withstanding this factor longer than the others. Partial damage to crist cells or vestibular nerve fibers should result in a change in characteristic shape, slope, and position relative to the graph's coordinate axes (horizontal shift) or a reduction in saturation level. This occurs because some of the components cease to take part in the formation of the generalized characteristic.

One can imagine that a decrease in characteristic slope, a shift in the characteristic along the horizontal, and, finally an upper limit on the characteristic may result from the death of part of the receptor elements or vestibular nerve fibers. A change in characteristic slope (at first increasing and, after a certain time, decreasing) may result from intoxication, which at first may apparently be accompanied by a certain brief sensitization of the receptor apparatus, and then by oppression. A change in characteristic slope and shape can also occur due to a disturbance in canal hydrodynamics or a change in cupula mechanical properties.

An isolated change in NC SI may probably occur upon dislocation of trunk formations, associated with NC suppression and partial death of neurons in the nuclei, as well as upon direct proximity to neurons in the nuclei of the center of inflammation, upon local disruption of blood supply and, finally, upon nonsymmetric exciting or inhibiting effects from hierarchically higher formations.

Note that only two indicators -- increased characteristic /166
slope and increased SI (if the latter occurs along with compensation mechanisms) -- are associated with increased NC EL level,

while all others are connected with its decrease. In reviewing the combinations of symptoms of a pathology during diagnostic use of the model, one must keep this situation in mind, since the co-existence of contradictory tendencies on the same side is unlikely.

Naturally, everything said about the causes underlying a particular pathology covered in the model can hardly be confirmed by any direct evidence. At the same time the validity of the assumptions made has been indirectly confirmed because, in most diagnostic research, when there was every reason to relate the origin of vestibular dysfunction precisely to a peripheral pathology, the set of deviations from the norm given above was quite sufficient to use the model [170]. On the other hand, when the model did not permit representation of conditions by which a particular BT result could be obtained (since model parameters calculated were contradictory), more careful study with additional input from other tests revealed the symptoms of central nervous system injury, i.e. these cases were clearly not included in the category of dysfunction for which the model had been developed.

Graphic Representation of the Model

The EL for each NC in the model may be represented as a graph. The diversity of EL's which cause nystagmus and determine its intensity is found as the difference in coordinates of the two EL's -- right and left.

Two graphs, corresponding to right and left NC, have an identical level for beginning to read coordinates on the Y-axis (cf. figure 46) along which EL's are plotted. Vestibular stimuli are plotted along the X-axis in conventional units. Zero on the X-axis corresponds to a state of rest for the receptor apparatus. The range of stimuli nominally designated 1 corresponds to stimuli when body temperature and irrigating fluid differ in temperature by $\pm 7^{\circ}C$. The positive stimulus is warm, the negative -- cool. The variable component (i.e. AF) as a function of stimulus is shown by the S-shaped curve. The scale is set so that AF's exposed to standard stimuli change within the limits of the straight part of the curve. The characteristic is limited from above by the saturation zone, and from below by the level of silence, which corresponds to the SI level. The silence level corresponds to complete cessation of AF movement along the nerve. In the norm, both nonlinear segments of the characteristic lie outside the zone in which the stimulus acts, but if there is a pathology, one of them may turn out to be within its limits: during type B pathology --

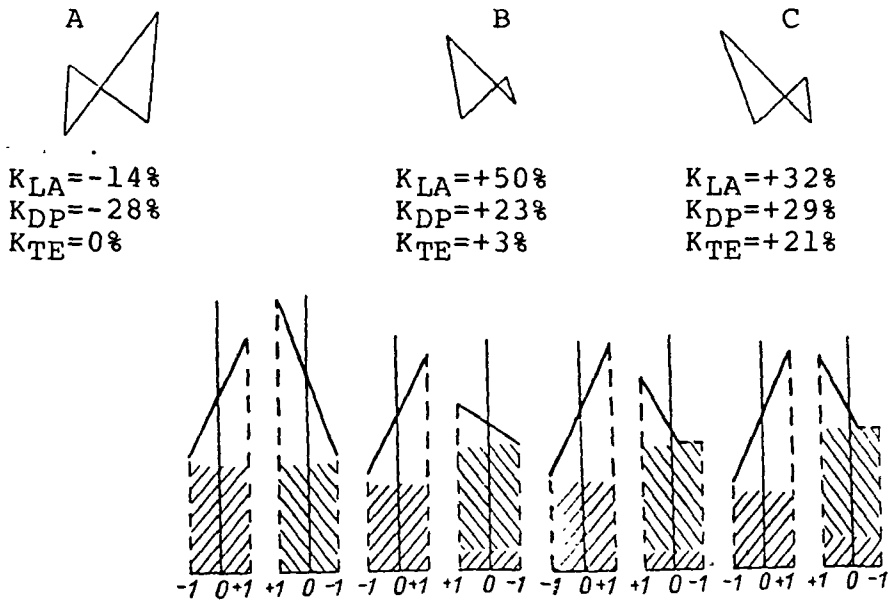

Figure 47. Model of BT if there is a pathology. Different diagram configurations (A-D) and corresponding diagnostic coefficients (in %) as a function of the pathology in the model (left pathology throughout).

A -- Increase in characteristic slope; B -- Decrease in slope, partial compensation (redistribution of SI shown by the broken line); C -- Horizontal shift with partial compensation; D -- Same shift, but with total compensation, by virtue of which the sign of K_{DP} changes.

between 0 and 1.0 on the X-axis, and with type C pathology -- between 0 and 1.0. Graphs are arranged as mirror images of one another. This is emphasized in the orientation of lateral semicircular canal receptors. Having plotted a unit on the stimulated side along the X-axis, we can determine the EL of a given NC during a caloric test, compare it with the EL of a second (untreated) NC, and find the difference, i.e. the equivalent of nystagmic intensity. In all cases, the difference in coordinates between right and left EL's is calculated. Therefore, a result with a positive sign denotes that nystagmus is directed rightward, while a minus indicates leftward nystagmus. This rule should be observed in the remaining cases as well (e.g. during calculation of K_{DP}).

Figure 47 shows the results which can be obtained at the model's outlet when a stimulus in each test travels to one labyrinth, while pathology exists only on one (the left) side. During each test, nystagmus intensity equals the absolute value of the differnce in EL coordinates for the right and left NC.

Model Behavior Given Various Deviations from the Norm /168

Let us consider in more detail the qualitative side of the model's behavior when the norm is ideal, i.e. when it is characterized by complete symmetry. We will trace the changes in diagram shape and the values of diagnostic coefficients (K_{LA}, K_{DP}, K_{TE}) when a particular pathology is assigned on the left (cf. figure 47). An increase in the characteristic's slope (cf. figure 47, A) results in negative K_{LA}'s and K_{DP}'s. A decrease in slope (cf. figure 47, B) creates conditions for positive K_{LA}'s and K_{DP}'s. As compensation is completed, the absolute value of DP drops to zero. Figure 47 C shows the effect of horizontal shift in the characteristic for partial compensaton, while figure 47 D shows compensation as complete. The compensation process caused a change in K_{DP} from +0.29 to -0.21. Compensation was not reflected in K_{LA} and K_{TE} values.

Once a particular form of pathological change is assigned, the model can be used to produce a rather wide variety of results actually obtained in diagnostic research (different diagram shapes, various combinations of K_{LA}, K_{DP} and K_{TE}), i.e. used to trace the mechanisms by which a particular result comes about. For example, a negligible horizontal shift in the left characteristic yields positive K_{LA} only. As shift increases, a positive K_{DP} develops, and as compensation begins, conditions are created for negative K_{DP}. Given upper limits of the left characteristic, K_{DP} is always positive. This list can go on.

The model shows particularly that the presence of compensation does not exclude the possibility that DP exists. This is, in principle, a critical conclusion which apparently explains in part those observations, familiar from practice, that DP's occur during BT's despite the absence of spontaneous nystagmus.

Not every combination of four reaction intensities out of those obtained at the model's output may be justified by these concepts in terms of mechanisms of nystagmogenesis during BT. For example, it is difficult to explain the co-existence on one side of two symptoms of pathology, of which one indicates intensified reactivity, while the other indicates oppressed reactivity, although formally these variations are possible and occur occasionally in practice.

What has been presented here can be considered as examples of using the model for didactic purposes: it has been shown that the results of BT's, superficially similar during evaluation in terms of K_{LA} and K_{DP}, may arise from various pathological deviations and it has also been established that the set of deviations permitted in the model is adequate to produce virtually any diagram shape and any K_{LA}/K_{DP} ratio at the

model's outlet.

Formalization of the Model and Aspects of Its Use in Diagnostics /169

The researcher in any specific diagnostic study has at his disposal four values for nystagmus intensity obtained during caloric BT tests. It is precisely in terms of these intensities that conditions for producing such results must be presented. Therefore, qualitative representations are inadequate for diagnostic use of the model.

The activity of each NC may be quantitatively characterized by the following properties: 1) the slope of the characteristic for AF as a function of stimulus, 2) the coordinate for the shift in characteristic along the horizontal (lower limit) or restrictions on the characteristic from above, and 3) vertical displacement of the NC energy level in terms of the EL of the opposite NC, caused, for example, by a change in the constant component (SI).

Since one labyrinth is exposed to stimulation in each BT test, the second may be considered untreated at that time. Hence vertical displacement takes part in formulation of a response to any test in the set and is, as it were, common to the two NC's, since its magnitude is not a function of whether the EL increases in one NC or decreases in another.

If the model is to be used unequivocally for diagnostic purposes within the limits of the assumptions made, the following limitations regarding deviations from the norm in terms of type B (or C) must be introduced. First, such a pathology is permitted only on one side. Second, no combination of type B and C pathologies is permitted, i.e. the characteristic may be limited from below or from above.

[illegible]ginal vertical shift in one NC activity graph [illegible]elative to another for the norm in diagnostic use [illegible]e model. Therefore, the results of the set of caloric [illegible]ests may be written as follows:

$$N_{rw} = K_r + \Delta,\ N_{rw} = K_r - \Delta,$$
$$N_{lw} = K_l + \Delta,\ N_{lc} = K_l + \Delta. \qquad (1)$$

where N is caloric nystagmus intensity during a warm (w) or cool (c) test to the right (r) or left (l); Δ is the portion of nystagmus intensity caused by the original difference between right and left NC EL, independent of stimulation; K_r and K_l are factors expressing the proportionality between nystagmus intensity and the magnitude of the stimulus for right (r) and left (l) vestibular apparati (the magnitude of the stimulus is set as 1). The symbols used in (1) to designate reaction intensity match those used above (cf. figure 44) for a, b, c, and

d. However, introduction of these new symbols is worthwhile. It emphasizes that only one nystagmometric characteristic (culmination SSC) is used for the model, just as others (e.g. nystagmus duration [570]) are often used to calculate K_{LA} and K_{DP}. /170

Equations (1) express reaction intensity both in the norm and in those cases of pathology when the characteristic's linearity is not violated.

If one characteristic is limited from below (type B) or from above (type C), intensities may be expressed by equations for one of the following particular models:

$$N_{rw} = RK_r + \Delta,\ N_{rc} = K_r - \Delta,\quad N_{lw} = K_l + \Delta,\ N_{lc} = K_l + \Delta. \qquad (2)$$

$$N_{rw} = K_r + \Delta,\ N_{rc} = RK_r - \Delta,\quad N_{lw} = K_l + \Delta,\ N_{lc} = K_l + \Delta. \qquad (3)$$

$$N_{rw} = K_r + \Delta,\ N_{rc} = K_r - \Delta,\quad N_{lw} = RK_l + \Delta,\ N_{lc} = K_l + \Delta. \qquad (4)$$

$$N_{rw} = K_r + \ ,\ N_{rc} = K_r - \Delta,\quad N_{lw} = RK_l + \ ,\ N_{lc} = RK_l + \Delta. \qquad (5)$$

where R less than or equal to 1 is a coefficient describing the level to which type B (or C) deviations are expressed.

Models (2)-(5) are distinguished by localized nonlinearity of the characteristic: in model (2) for example, the nonlinearity exists in the upper (warm) part of the right characteristic, while in model (5) nonlinearity is expressed in the cool reaction to the right. The magnitude of R in the latter case coincides with the point on the X-axis at which characteristic AF becomes horizontal and crosses into the silence zone, since AF ceases at a stimulus less than -1.0.

When approaching diagnostic research, one should first determine whether the pathology in the case is type B or C, i.e., on which side the nonlinearity occurs, if it occurs.

The criterion which makes it possible to answer the first question is K_{TE}, calculated as the ratio of the difference in intensity of warm and cool reactions to their sum:

$$K_{TE} = [(N_{rw}+N_{lw})-(N_{rc}+N_{lc})]/[(N_{rw}+R_{lw})+(N_{rc}+R_{lc})] \qquad (6)$$

From calculating K_r, K_l is greater than zero and R is less than or equal to 1. Therefore the following inequalities are valid for K_{TE}'s corresponding to models (2), (3), (4), and (5):

$$K_{TE(2)} = K_r(R-1)/K_r(R+1)+2K_1 \leq 0;$$
$$K_{TE(3)} = K_r(1-R)/K_r(R+1)+2K_1 \geq 0;$$
$$K_{TE(4)} = K_1(R-1)/K_1(R+1)+2K_1 \leq 0;$$
$$K_{TE(5)} = K_1(1-R)/K_1(R+1)+2K_r \geq 0.$$

Consequently, when K_{TE} does not equal 0, the pathology is of type B (or C), but when K_{TE} does equal 0, there is no restriction on the characteristic and stimuli of ± 1.0 act within the limits of its linear segment. Type B pathology causes K_{TE} greater than 0, and with type C pathology, K_{TE} is less than 0.

TABLE 18 /171
EQUATIONS FOR CALCULATING MODEL PARAMETERS AS A FUNCTION OF K_{TE} AND THE SIDE OF INJURY

Parameter	$K_{TE}=0$ (7)	$K_{TE}=0$ Right-side pathology (8)	$K_{TE}=0$ Left-side pathology (9)
Δ	$(N_{rw}+N_{lw})-(N_{lw}+N_{rw})/4$	$(N_{lc}-N_{lw})/2$	$(N_{rw}-N_{rc})/2$
K_r	$(N_{rw}+N_{rc})/2$	$N_{rw}-\Delta$ (when $K_{TE}>0$) $N_{rc}+\Delta$ (when $K_{TE}<0$)	$(N_{rw}+N_{rc})/2$
K_1	$(N_{lw}+N_{lc})/2$	$(N_{lw}+N_{lc})/2$	$N_{lw}+\Delta$ (when $K_{TE}>0$) $N_{lc}-\Delta$ (when $K_{TE}<0$)
R	No restrictions	$\frac{(N_{rw}+N_{rc})}{K_r}-1$	$\frac{(N_{lw}+N_{lc})}{K_1}-1$

Table 18 presents equations intended for practical calculation of models during diagnostic research as a function of K_{TE} and the side of injury.

The model is used for diagnostic work in the following sequence. BT results -- culmination SSC's -- are best inserted into the table first and represented in the form of diagrams. In and of itself, representing BT results as diagrams provides no additional information of any sort, but is sufficiently descriptive. As experience is accumulated in working with the model/diagram combination, the nature of the pathology can be successfully represented in terms of just one type of diagram.

Then K_{LA}, K_{DP}, and K_{TE} are calculated. These calculations (cf. figure 45) are required in any diagnostic study.

Then, regardless of whether indications of deviation from the norm are observed in the first stage, model parameters should be calculated with equations in table 18. Whether there is a deviation should be determined by comparing the results of calculations with the statistical description of model parameters in the norm given in table 19. After model parameters are calculated, it is expedient to plot graphs which clearly reflect the relationship between the EL's of the two NC's.

When K_{TE} does not equal 0 and the injured side is unknown, both hypotheses are tested, i.e. model parameters for both right and left pathologies are calculated. If the difference between these two alternatives is negligible, then it makes virtually no difference which alternative is preferred, since either gives a qualitative representation of the nature of the process. If the difference between them is great, then one of them must be rejected because of formal considerations or on the basis of additional data. The latter includes data on anamnesis, otoscopies, audiometry, et al., but if these are inadequate, the test can be conducted using additional research which will be discussed below. /172

TABLE 19
MODEL PARAMETERS (RESULT OF STATISTICAL PROCESSSING OF THE NORM IN 50 HEALTHY SUBJECTS)

Parameter	n	x	Norm boundaries at 5% significance by distribution)
K_{TE}	50	0.029 ± 0.011	-0.080 - +0.160
Δ	50	-0.46 ± 0.18	± 3.0
K_r, K_l	100	22.3 ± 0.55	13.0 - 33.0
$(K_r-K_l)/(K_r+K_l)$	50	0.0064 ± 0.0076	± 0.10

In all cases, one must rely on the absolute values of SSC and statistical information obtained in material on the norm.

So far the norm has been the state of complete balance between NC energy levels resulting from identical characteristic slope, from equal SI's, and from the lack of limitations on the characteristic (violation of linearity), i.e. a certain ideal state. In addition, it is well known that for virtually healthy people, complete symmetry of caloric reactions is rather the exception rather than the rule. Required model parameters were evaluated in terms of BT results for 50 healthy humans, published in 1958 [502], since the sample of subjects in this study is sufficiently uniform and the BT procedure corresponds to that most widely used in practice worldwide [230]. Raw numerical data for calculating model parameters was data on

culmination SSC. Processing this material using model equations gave an understanding of what the limits of physiological fluctuations in model parameters were and comparison of these results with data obtained from other samples showed an entirely satisfactory correlation.

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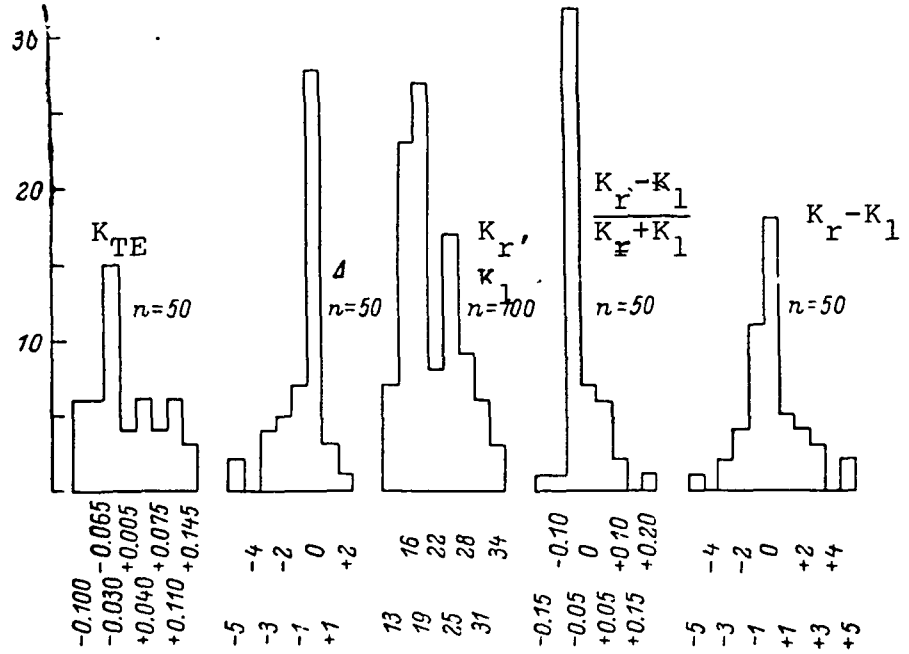


Figure 48. Model parameters in the norm (from [124]).

X-axis -- Lower boundaries of classes; Y-axis -- number of dates. K_{TE} -- thermostimulation effectiveness; Δ-- difference in EL's in right and left NC's; K_l, K_r --coefficients of proportionality evaluated as the slope of the linear segment of the AF characteristic; $[(K_r-K_l)/(K_r+K_l)]$ -- relative difference in coefficients; K_r-K_l -- absolute difference. Sample size -- 50 BT's.

Table 19 presents arithmetic means and standard deviations for K_{TE}, as well as the difference in EL's for right and left NC's (Δ), characteristic slope coefficients (K_r, K_l), and their relative difference $(K_r-K_l)/K_r+K_l)$. It follows from hypotheses made when the models were constructed that distributions of K_{TE}, Δ, and the difference K_r-K_l should have null averages. The probabilities of obtaining the standard deviations for K_{TE}, K_r and K_l in the table with null averages are 0.014, 0.015, and 0.4 respectively. Consequently, the model of the norm does not contradict experimental data at 1% significance. Figure 48 shows histograms for model parameter distribution in healthy humans.

Concepts of normal model parameters are required for valid conclusions on the definite presence of a pathology, as well as for selecting one of the two alternative models (and, correspondingly, rejecting the other) when it is difficult to choose the injured side.

Sometimes K_{LA} and D_{DP} values in and of themselves evidence the definite presence of vestibular dysfunction. In these cases, the model makes it possible to clarify the origin of the dysfunction. However, it is often impossible to make such observations when definite vestibular dysfunction is not apparent from K_{LA} and K_{DP} calculations. Then the model is useful, since in several such cases it can be used to identify dysfunction in terms of the absolute values of K_r and K_l, in terms of the relative difference in these values, and in terms of Δ. /174

The possibilities for using the model in diagnostic work are of course not infinite. Note that the model is intended primarily for unilateral pathology. Further, the model encompasses only the receptor apparatus, nerve, and vestibular NC levels, i.e it does not permit evaluation of the nature of an injury localized on a higher level.

Below are examples of using the model in diagnostic research.

Patient I, aged 49, was subjected to comprehensive examination [98] in the Leningrad Scientific Research Institute for Otorhinolaryngology and then in a neurosurgical hospital, as a result of which an initial diagnosis was made: arachnoiditis of the left cerebellopontile angle. Two years later, due to his deteriorating condition, the patient was again examined and another diagnosis made: neuroma of the right statoacoustic nerve. Data from two BT's conducted at a 2-year interval make it possible to compare model parameters and to evaluate the dynamics of the pathological process (cf. figure 49). In terms of data from the first test in 1979, standard evaluation of results [268] revealed asymmetric reactivity in the form of right-side hyporeflexia (K_{LA}=-25%). The model provided additional information: the definite difference in terms of the slope of right and left characteristics (-24% given a norm of 10%), and complete compensation. The condition had changed drastically by the time of the second BT (1981): labyrinth asymmetry deepened (K_{LA}=-30%); directional preponderance developed (K_{DP}=-58%); and warm tests had clearly become more effective than cool (K_{TE}=+20%), which demonstrated the development of nonlinearity in the cool segment of one characteristic. The model made it possible to clarify the condition of the vestibular

function: decompensation (Δ=-6 with a norm of $\pm$3: cf. table 19), caused by a restriction from below on the right characteristic (type B pathology, cf figure 46). Note that K_r and K_l remained virtually unchanged. The correspondence of K_l's obtained during the first and second studies indicates that no changes occurred on the left over the time between the two BT's: despite the fact that the intensity of each nystagmus caused by stimulation of the left (healthy) ear varied, the sum of these intensities remained as before.

Here is another example.

Patient K, aged 28. After comprehensive examination conducted in the Leningrad Scientific Research Institute for Otorhinolaryngology, a neuroma of the left statoacoustic nerve was removed from the patient. BT results are given in figure 50. The example shows how the model can be used with spontaneous nystagmus. Spontaneous nystagmus was directed rightward (toward the healthy ear) and had an SSC equal to $10^{\circ}\cdot sec^{-1}$. Warm stimulation to the left did not cause a typical response: instead of the anticipated nystagmus on the left, a nystagmus to the right was recorded (SSC=$5.0^{\circ}\cdot sec^{-1}$). This fact is noted in the table of BT results by the fact that intensity N_{lw} has a minus sign. The warm test on the right is thus accompanied by only inhibition of the rightward spontaneous nystagmus. K_{LA}, K_{DP}, and K_{TE}, as well as model

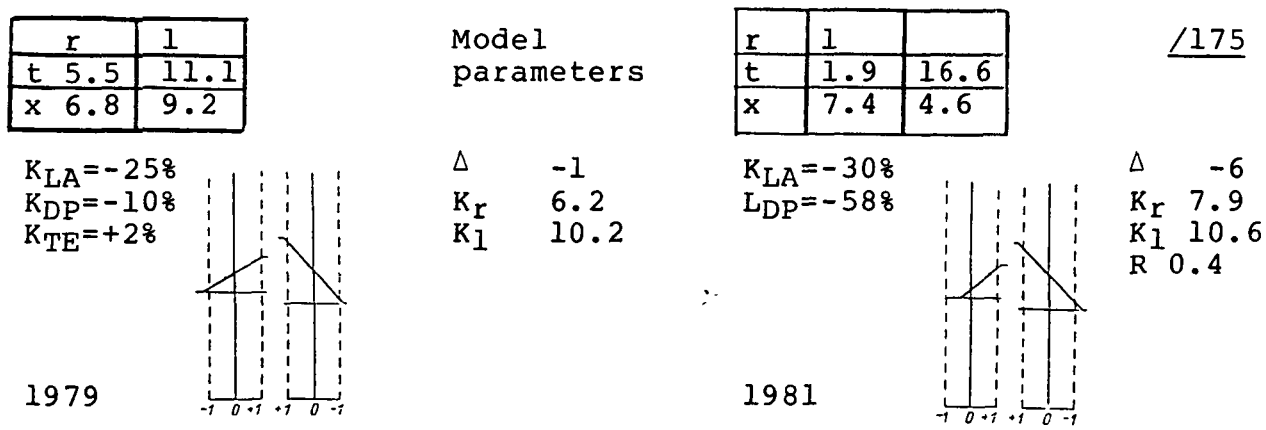
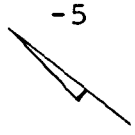


Figure 49. Diagnostic use of the BT model during two-stage examination of a patient over 2 years (concluding diagnosis: neuroma of the right statoacoustic nerve).

Changes in caloric nystagmus intensity, observed in left-side tests in the second BT were caused by an increase in pathological changes on the right side. Remaining explanations are given in the text.

parameters, were calculated with regard for the unusual sign of the reaction produced during the warm test on the left. The results of calculation are: K_{LA} = +64%, K_{DP} = +100%, K_{TE} = +27%; Δ = +11.5, K_r = 13.3, K_l = 5.5, R = 0.

	r	l
t	25.0	-5.0
x	2.0	10.7



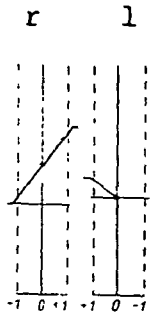


Figure 50. Diagnostic use of the BT model (diagnosis: neuroma of the left statoacoustic nerve).

The model was used with spontaneous nystagmus on the right (SSC = $10^{\circ}\cdot sec^{-1}$). A warm test to the right was associated with inhibition of spontaneous nystagmus. The result of this test is shown with a minus sign in the table. Remaining explanations are given in the text.

The model made it possible to supplement the formal conclusion of hyporeflexia on the left with information on the nature of the pathology (a significant shift in the left characteristic, as indicated by the fact that R = 0) and on the substantial decompensation (Δ = 11.5, which exceeds the normal permissible value by a factor of three). The model made it possible to understand the cause for low nystagmus intensity during the cool test on the right (on the healthy side): the initial EL of the right NC was considerably higher than that on the left. One might assume that the significant shift in the left characteristic, because of which the characteristic completely lacked a cool segment, was the result of the death of some of the statoacoustic nerve fibers.

Determining the side of the injury presented no difficulties /176 in either of the examples considered, since it could be judged in terms of other symptoms. However, note that in practice there may be cases when the injured side may be difficult to determine either from indirect data or from the absolute values of nystagmometric characteristics. We might imagine that, when K_{TE} is less than 0, i.e. given an indication that there is a horizontal shift in one characteristic, it is difficult to determine on which sign this shift is taking place. In similar situations parameters for both hypotheses (shift rightward and

leftward) should be calculated first. In most cases one alternative can be rejected at this stage on the basis that, otherwise, unmatched signs would be permitted to co-exist. If uncertainty still remains at this stage, an additional cool test with irrigating fluid at 20°C should be conducted. If cool nystagmus intensity in this case is the same as that at 30°C, shift occurs on the given side.

Possibilities for Using the Model in Ambulatory Practice

Obviously, the information value of diagnostic tests depends substantially on the extent to which a quantitative approach is used to evaluate reactions. The use of a model directly related to electronystagmography has been described above. Since electronystagmography is rarely used in ambulatory examinations and visual evaluation of nystagmus hinders introduction of quantitative procedures, attention should be given to a compromise solution adapted to conditions of visual observation.

Usually when frequency is being evaluated during visual observation, one speaks of nystagmus as "rare," "moderate," or "frequent." Evaluating amplitude, one uses definitions such as "small swing," "moderate swing," and "wide swing." In other words, in all cases one should try to give the most detailed possible description of the reaction observed. The point of the proposed procedure is to replace a verbal description with evaluation by assigning points.

The technique is based on the fact that the product of two nystagmometric characteristics -- frequency and ampltiude -- has a speed dimension ($^{\circ}\cdot sec^{-1}$), while, in meaning and in absolute value, this product is close to a more important char-

TABLE 20 /177

SCALE SCORING NYSTAGMUS INTENSITY BY POINTS DURING VISUAL OBSERVATION AND AN EXAMPLE OF USING POINTS WHEN CALCULATING DIAGNOSTIC COEFFICIENTS IN TERMS OF RESULTS

Verbal Description	Frequency Impacts per 10 sec	Points	Verbal Description	Amplitude* Movement swing, mm	Points
"Rare"	To 17 inc.	1.0	Small swing	Less than 2	1.0
	18-20	1.5			
"Average"	21-23	2.0	Moderate	2-3	2.0
	24-27	2.5	swing		
"Frequent"	27 or more	3.0	Large swing	More than 3	3.0

*For convenience, amplitude is expressed in millimeters shift for a point located on the surface of the eyeball (calculated with regard for "average" eye dimensions).

acteristic -- SSC. Using this product to evaluate nystagmus intensity was first suggested by Ohm [481] who called the characteristic "energy." A verbal description of frequency and amplitude can be replaced by evaluations by points, i.e a measure of nystagmus intensity entirely suitable for comparing reactions. The scale for this evaluation [121] is proposed on the basis of statistical research on norms for caloric nystagmus [129]. The simplest is a three-point scale in which the average (2 points) corresponds to the arithmetic mean for the characteristic obtained in the norm. To increase the accuracy of the result somewhat, the frequency evaluation scale can be graduated in fractions (cf. table 20). Point evaluation of nystagmi produced during BT's can be used to calculate K_{LA} and K_{DP}. An example of evaluating a BT in points follows.

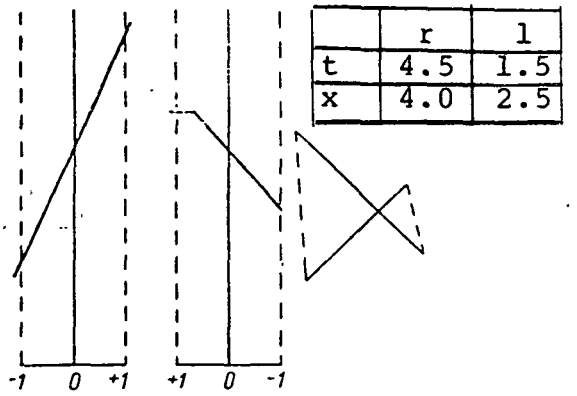
	Right Ear	Left Ear
Warm	Frequency -- 20 impulses per 10 sec (1.5 points) Amplitude -- more than 3 mm (3 points) Intensity = 1.5x3.0= 4.5 points	Frequency -- 19 impulses per 10 sec (1.5 points) Amplitude -- less than 2 mm (1 point) Intensity=1.5x1.0= 1.5 points.
Cool	Frequency -- 22 impulses per 10 sec (2 points) Amplitude -- 2 mm (2 points) Intensity = 2.0x2.0= 4.5 points	Frequency -- 26 impulses per 10 sec (2.5 points) Amplitude -- 1 mm (1 point) Intensity=2.5x1.0= 2.5 points.

K_{LA} = [(4.5 + 4.0) - (1.5 + 2.5)]/(4.5 + 1.5 + 4.0 + 2.0) = +36%
K_{DP} = [(4.5 + 2.5) - (1.5 + 4.0)]/(4.5 + 1.5 + 4.0 + 2.0)= +12%
Formal conclusion: Hyporeflexia on the left.

In all cases when using diagnostic coefficients (K_{LA} and K_{DP}), one should remember that the relationship between the level of asymmetry and the actual change in nystagmus intensity is not linear [513]. It is especially important to account for this circumstance in evaluating by points, since K_{LA} and K_{DP} values obtained with this method and deviations from the norm in terms of absolute values of nystagmometric characteristics /178 cannot be compared.

The result of assigning points can be used also to construct a diagnostic model. In the example, the sum of thermal reaction intensities is less than the sum of cool intensities. Consequently, it must be assumed that one characteristic is restricted from above. Since K_{LA} is greater than 0, it is natural to assume the presence of a pathology on the left and to calculate model parameters using equations in the last column in table 18. Despite the relative nature of these evaluations and their unquestionably lower accuracy (as compared with evaluations in terms of ENG's) the model has made it possible to supplement the formal conclusion of hyporeflexia on the left with the fact that the hyporeflexia is caused by a decrease in

the slope of the curve for the left AF and by a restriction from above on the left characteristic (cf. figure 51). Understandably, one must keep in mind that the parameters for this model, calculated using a point system, differ from those in table 19. Of all the model parameters calculated using the point system, only the relative difference $(K_r - K_l)/(K_r + K_l)$ is suitable for comparison with the norm. In the example shown it is 30%.



	r	l
t	4.5	1.5
x	4.0	2.5

Figure 51. Example of constructing a diagnostic model from results of a BT conducted with visual evaluation of nystagmic reaction intensity on a point scale.

Remaining explanations appear in the text.

$\Delta = (N_{rw} - N_{rc})/2 = (4.5 - 4.0)/2 = 0.25$
$K_r = (N_{rw} + N_{rc})/2 = (4.5 + 4.0)/2 = 4.25$
$K_l = N_{lc} - \Delta = 2.5-0.25 = 2.25$
$R = [(N_{lw} + N_{lc})/K_l] - 1 = [(1.5 + 2.5)/2.25] - 1 = 0.7$

Use of the model in practice showed that it is suitable for diagnosing vestibular dysfunction at a statistically reliable level, particularly when traditional evaluation of BT by calculating LA and DP did not permit definite determination of a deviation from the norm.

Use of the Model to Study the Mechanisms by Which Directional Preponderance Originates in Nystagmus

The model was used as the basis for predicting the results of experimental research. The reason for the research was that it was observed in a basic experiment that cool nystagmus slows when exposed to additional ipsilateral stimulation by sound vibrations carried to the ear by vibration transmission through bone [189]. Further studies [136, 137] were devoted to using the model to define the most probable level at which this phenomenon would occur, as well as possible mechanisms for its occurrence. /179

Two alternative hypotheses were initially subjected to testing: a) the direct effect of aural stimulation on the receptor apparatus of the semicircular canal and b) the indirect i.e. via the auditory system (including its central representation), efferent effect on labyrinth receptors or on nystagmogenic formations.

The first hypothesis was checked experimentally. The working hypothesis consisted of the following. Exposure to sonication creates NC energy level asymmetry: the ipsilateral NC produces a certain overbalance and creates a background of increased (as compared to the level outside the test) activity. The background is the cause of the change in the caloric reactions. The proposed mechanism through which a background inhibiting cool nystagmus originates [189] is assumed to be the physical phenomenon described as differential cupular deviation. Differential cupular deviation was observed in a study on cupuloendolymphatic shift in a physical model of a labyrinth [49, 164, 165]. It was established that sign-variable periodical vibrations acting through the endolymph trunk cause a gradual buildup of residual utriculopetal cupula deviations. This proceeds by virtue of the unequal conditions under which the cupula shifts in opposite directions: the anatomical structure of the ampulla, and the different diameters of the openings connecting it to the vestibule and the canal make it easier for utriculopetal shifts to predominate somewhat over utriculofugal. Differential cupula deviation may be rather great -- a particular case is differential cupula superdeviation in which cupula vibrations after a certain time proceed along one side from the cupula's initial position, i.e. as if around a new zero, shifted utriculopetally (cf. figure 52).

This information, the initial condition caused by preliminary sonication of the right labyrinth, served as the basis for assuming a certain primordial utriculopetal cupular deviation caused by endolymph oscillations directed along the canal and continuing for a rather extended period. Given this assumption, even before the caloric test begins, right NC EL should be higher than left (cf. figure 53) because the ordinary AF_{sp} level is enhanced by a certain portion of the AF caused by the change in the position of the cupula of the sonicated (right) canal. In other words, an initial shift of the zero along the X-axis in the utriculopetal direction was assumed. /180

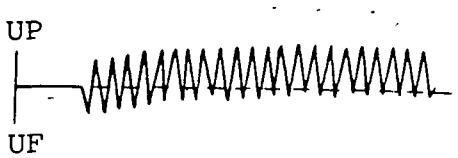


Figure 52. Differential cupula superdeviation (from [49]).

X-axis -- Time; Y-axis -- Utriculopetal (UP) and utriculofugal (UF) cupula deviations during exposure to periodic oscillations.

Since SI in the nuclei are identical (we have in mind the normal state of the NC), only AF curves are shown on the graphs for simplicity. This model may be subjected to each of four caloric tests and the changes in reactions as compared to the norm and how the relationship of intensities comes about can be evalua-

ted. The initial right NC EL is increased. Warmth from the /181
right intensifies the right AF, which, added to the increased background, causes nystagmus on the right, with an intensity exceeding the norm by a certain amount. In contrast, the cool test on the same right ear produces a weakened reac-

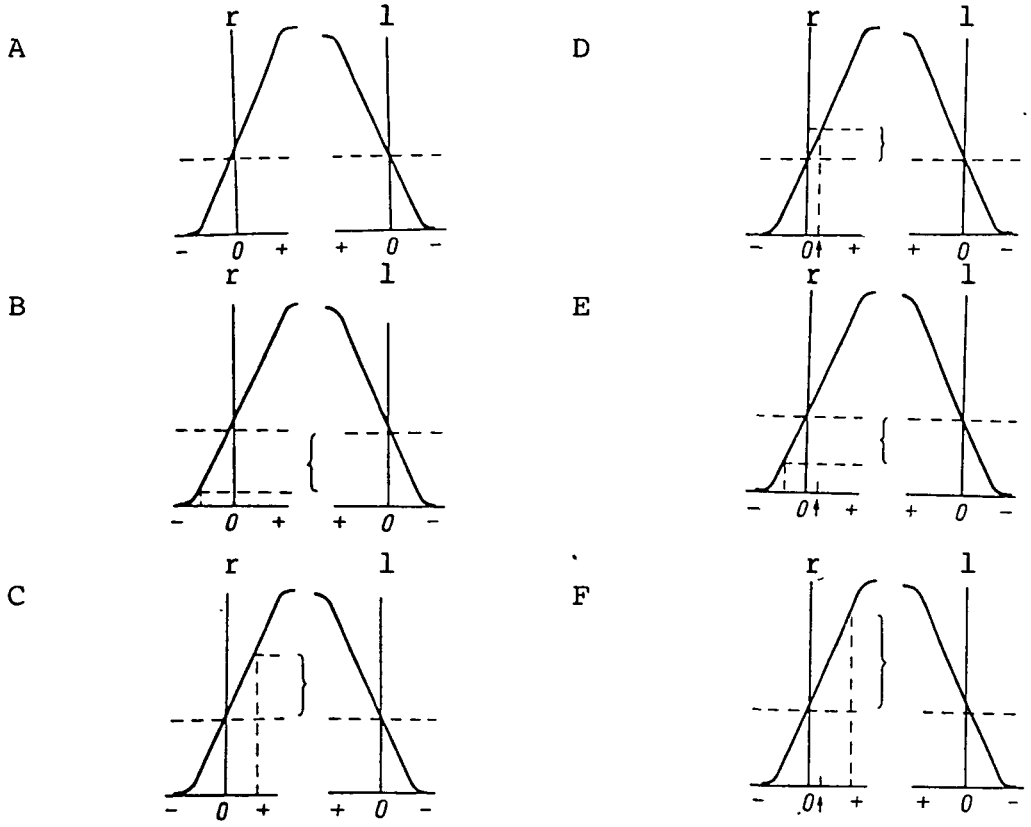


Figure 53. Hypothetical mechanisms of the phenomenon of directional preponderance during exposure to a sound stimulus (bone conduction, 1000 Hz) in one labyrinth (from [137]).

The effects of caloric stimulation of the right (r) labyrinth with the left (l) untouched under ordinary conditions (A, B, C) and on a background of additional sound stimulation (D, E, F) are shown. On A and D -- initial conditions. X-axis -- utriculopetal (+) and utriculofugal (-) cupuloendolymphatic shifts (arrow on D, E, F designates background shift caused by differential cupula superdeviation -- cf. figure 52). Y-axis -- afferent flows (inherent activity levels are not shown, since there is no data on their involvement). Brackets denote the differences in energy level of vestibular nuclei during cool (B and E) and warm (C and D) tests on the right labyrinth, as well as the background difference (D).

tion because the reduction in AF caused by cooling progresses not from the normal AF_{sp} level, but from an increased background level. Despite the identical absolute intensity of the caloric stimuli, the utriculopetal deviation in the right cupula with a warm stimulus is thus greater than the norm, since it will be added in with the deviation produced even before the labyrinth sonication test. At the same level, utriculofugal deviation of the right cupula is reduced (as compared with the norm) during a cool test, since the energy of the endolymph shift will in part be expended in overcoming the initial (caused by sonication) utriculopetal differential cupula deviation.

Other relationships develop during caloric tests on the left ear: a cool test causes a reaction stronger than the norm, while a warm test produces a weaker one. This occurs only by virtue of the fact that the promordial right NC EL is somewhat higher than the left. The amount by which nystagmus should change is noted in figure 54 as F (background).

The shape of the diagram during tests with sound should, of course, differ from normal: each axis on which rightward reactions are plotted is longer by the value F. The two other axes, in contrast, should be shorter by the same amount. This prediction has been confirmed by experiment.

The following caloric test procedure was used: 150 ml of water, injection time 40 sec, water temperature 30°C or 44°C. Sound stimulus: a 1000-Hz tone, intensity 60 dB (above the average threshold of an adult). Sound began 60 sec before the caloric test. It ended upon cessation of the nystagmus. The sound traveled through a vibrator (bone conduction) on the mastoid process of the right ear. Each caloric/sound test was matched to a standard caloric test which either preceded or followed the sound test. This alternation, as well as intervals between tests of less than 30 min, made it possible to minimize the effect of adjustment. The intensity of each reaction was evaluated in terms of average SSC in the nystagmus culmination segment.

Since conducting eight tests on one subject involves an excessively high load, in most cases only two tests were run (one with sound, the other without) and, if it was necessary to conduct more tests, a one or two day break was imposed. To reduce the effect of individual spreads on the results -- which is inevitable given the nature of the experiment -- the absolute values of SSC's were calculated in pairs of like caloric tests, one of which was conducted on the sonicated labyrinth. Then the difference in these values was found. /182

A combined result was obtained from 112 ENG's (56 pairs) recorded in 45 children aged 4 to 8. All subjects were included in the test group only if the otoscopic picture was normal and otiatric and neurological anamnesis were positive.

The result of the study in the form of arithmetic averages and their errors for each of the four samples is presented in table 21. Each figure in this table was obtained by statistical processing of one of the four samples. Each sample

	Right	Left
44°C	A	B
30°C	C	D

	Right	Left
44°C	A+F	B-F
30°C	B-F	D+F

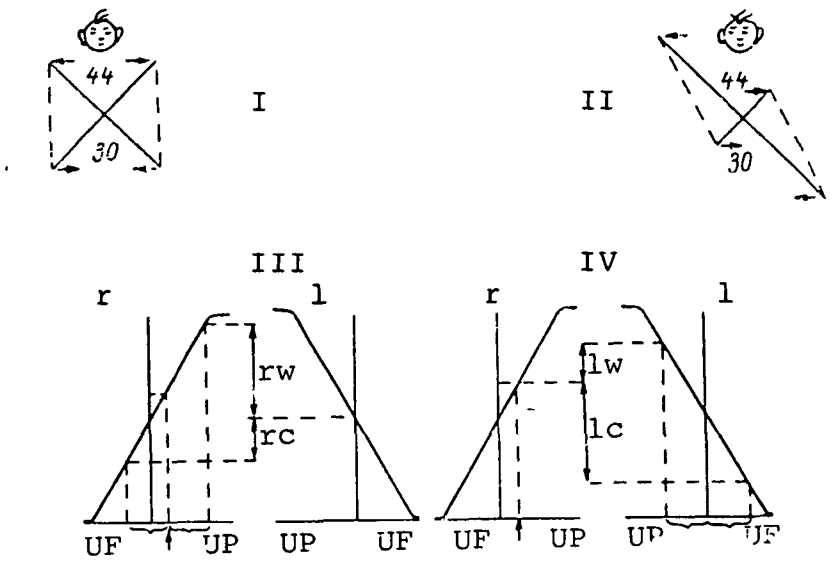


Figure 54. Change in caloric reactions upon labyrinth exposure to sound (from [136]).

I -- BT in the norm: A, B, C, and D -- nystagmus intensities; II -- BT with right labyrinth exposed to sound; background asymmetry is involved in each sample in the form of a correction (F) to intensity: conditions for K_{DP} greater than 0 are created. II -- Formulation of reaction during right-side tests. The arrow indicates background utriculopetal (UP) cupula deviation; initial EL of the right NC predominates over left; equal caloric stimuli cause identical cupula deviations (denoted by brackets), but, as a result of the initial deviation, utriculopetal displacement predominates over utriculofugal (UF); rw -- difference in two EL's during a warm test; rc -- same during a cool test. IV -- caloric tests on the left ear; lw -- difference in EL with a warm test; lc -- same during a warm test.

consisted of differences found between paired ENG's, i.e. recorded in the same subject during two identical caloric tests, one of which was accompanied by sound. /183

Obviously, the result correlates satisfactorily with the predicted model: nystagmus intensity changed in each test when a labyrinth was exposed to additional sound stimulation. All changes took place in the direction predicted. In no case did the result contradict the prediction in terms of the sign of the changes, although individual variations in absolute values occurred (especially during caloric tests on the unsonicated side). The unambiguity of the results obtained was to some degree probably a function of features related to subject age. Childhood is characterized by high vestibular system reactivity [412, 555].

TABLE 21
DIFFERENCES BETWEEN NYSTAGMIC REACTION INTENSITIES, EVALUATED IN TERMS OF AVERAGE SSC INTERVALS, IN PAIRED ENG's FROM FOUR SAMPLES ($\bar{x} \pm m$, $^\circ \cdot sec^{-1}$) [136]

Stimulus	Right Ear	Left Ear
Warm	5.1 ± 0.5	5.3 ± 1.6
Cool	6.2 ± 0.4	7.1 ± 2.2

Averages in terms of samples of differences turned out to be rather high, which justifies the statement that, in a particular way, these averages are equivalent to evaluation of a background caused by increased NC activity on the sonicated side.

The effect of sound in these experiments was evaluated as a mechanical, vibratory effect. Naturally, all that which has been said about mechanisms underlying the phenomenon remains only hypotheses. For the time being direct confirmation in any kind of physiological experiment is impossible.

Several studies have been devoted to the effect of vibration on the vestibular function. These were works primarily electrophysiological in nature (cf. for example [160, 198]). Studies on man in most cases have a hygienic purpose [188]; experimental work is more rare. The possibility of vibration affecting the vestibulosensory and vestibulo-oculomotor reaction in man has been noted. In particular, it has been established that a latent spontaneous nystagmus may be discovered if the mastoid process is exposed to vibration [435]. It has been shown that a vibrator used in physiotherapy can be used to produce the effect of vestibular stimulation in the form of

visual and postural illusions, symptoms of motion sickness and, /184
sometimes, nystagmus [415] in an adult human. The vibrator in these experiments was used for a long time (about 1 hr) to various parts of the head; frequency equaled 120 impulses per second. Horizontal nystagmus developed upon stimulation in the area of the mastoid process or the zygomatic arch. The authors state that vibration stimulation -- in contrast to the bilateral effect of exposure to angular acceleration -- produces a monolateral effect.

Sound traveling through a bone conductor unquestionably acts on the cochlea. Can stimulation of the cochlea produce a change in the vestibular apparatus? A study on six apes [397] was conducted in relation to an electrode hearing prosthesis. One exhibited nystagmic eye movements in response to electrical stimulation of the cochlea. Intense (125 dB) acoustic stimulation by a tonal signal (100-5000 Hz) may cause a human to sense that his field of vision is shifting -- the greatest effect being at 500-1000 Hz [493]. Note that the attempt to observe nystagmus during exposure only to sound (without calorization) was unsuccessful [136].

A satisfactory correspondence of experimental results and those predicted by the model cannot, of course, be considered basis for asserting that the peripheral mechanism by which a sound signal affects nystagmus is singular, i.e. that other mechanisms, including those modulated by the auditory system, are excluded.

Sound traveling through a bone conductor acts on the cochlea, from which signals travel to auditory centers. Then centrifufal effects both on the vestibular receptor apparatus and on nystagmogenic centers may develop. In particular, an action changing the threshold value may occur along the efferent paths to the labyrinth. One might assume that, upon sonication, the threshold would increase, which would result in a situation in which cool stimulus, which previously had caused rather intense nystagmus, would be less effective and the reaction would be weakened. But how can the intensification of warm nystagmus during a test on the same ear be explained? How can one explain changes in nystagmic reactions in the opposite (unsonicated) ear? Apparently, some efferent effects on the labyrinth are inadequate to cause the effects observed. One might consider another alternative of modulated effects, assuming that unlike signals ultimately causing a change in nystagmus intensity travel from the auditory centers not to labyrinth receptors, but to a certain nystagmus center. This effect may be either exciting or inhibiting. Since, during a cool test on the right (sonicated) ear, nystagmus intensity is already decreasing, the effect should be considered inhibiting. However, during a warm test on the same ear, nystagma intensifies. To explain this result one must assume that, this time, the effect of the same /185
sound signal on the same centers for some reason became excit-

ing. It is difficult to imagine how central mechanisms must be reconstructed each time to ensure effects from a change in nystagmic reaction intensity which differ in meaning depending on the type of vestibular stimulus (warm or cold) and the stimulated side (sonicated or unsonicated).

Naturally, when the relationship of receptor systems is studied, attention must be given primarily to central mechanisms, but the involvement of these mechanisms can hardly be explained by the diversity of facts in this case. A change in nystagmus due to the effect of additional sound stimulation, at first actually a manifestation of high-level receptor systems, is ultimately a more simple phenomenon caused by the direct effect of sound on vestibular apparatus receptors.

One might say that the experiment with sonication artificially produced a receptor condition which should be regarded as yet another variant of pathology not previously provided for by the model. By itself, this variant was a successful experimental model of directional preponderance peripheral in origin [120] and, from this standpoint, it may be interesting for fundamental vestibulometry.

The following two questions arise as a result. First, can such a pathology be represented in reality? Second, if such a pathology is possible, then can the peripheral genesis of directional preponderance be identified in such an instance (i.e. when $K_{LA} = 0$) in terms of any indicators?

One might imagine that a certain similarity might be expected with cupulalithiasis, which is recently becoming more and more a subject of debate in literature (cf. e.g. [179, 230, 233]). The nature of this pathology is that the cupula develops deposits whose density exceeds that of the cupula itself. Literature offers no direct indications of the possibility of cupulolithiasis in the lateral canal ampulla. However, if this possibility is assumed, one might imagine that, when the head changes position (e.g. if the head tilts in the sagittal plane), this cupula will deviate and conditions similar to those which occur during sonication will arise, i.e. AF will change on the side of the cupulalithiasis. The sign of this change will depend on the patient's position (supine, pronate).

Prospects for Using the Model

Using the model to study mechanisms of the phenomenon of directional preponderance in its various manifestations is a distinct possibility. In particular, the phenomenon of /186
weakening of nystagmus resulting from repeated nystagmi in the same direction may formally be considered as one of the manifestations of directional preponderance. Consequently, the model may be useful in studying it. Further, the model may facilitate an increase in the information value of rotatory

tests, which is still insignificant. Formally speaking, any asymmetry in a pair of nystagmi of different direction caused by an adequate stimulus -- angular acceleration -- may be regarded as a manifestation of DP, since changes in two afferent flows are involved in formation of each reaction. Changes in one of them can be viewed as similarly originating in a warm test, the other in a cool test. The intensity of rotatory nystagmus directed to the right can be taken as equal to the sum of the intensities of two reactions -- to warmth on the right and to cold on the left. Consequently, the difference in intensities of right- and leftward post-rotatory (or rotatory) nystagmi indicate the presence of DP, while the ratio of intensity differences to sums is a measure of DP [149]. Naturally, for the time being we can speak only of a qualitative similarity, but this does not detract from the essential point. The most important fact is that any rotatory test which results in a pair of nystagmograms cannot in principal provide information on the status of the vestibular function in a quantity greater than could be obtained if the entire evaluation of BT results were limited to calculation of K_{DP}, whose diagnostic value is still minor. At the same time, DP deserves more attention as the facts presented below will demonstrate. Humans systematically exposed to noise and vibration in a plant more often exhibit asymmetric nystagmus intensity caused by angular acceleration [149] (as compared with a control). This asymmetry is unstable in its absolute value and even in sign. This was discovered in a comparison of results from two studies: before the working day began and at its end. Central mechanisms are the most likely participants in DP changes of this type, but peripheral dysfunctions which may exist in an ambiguous form cannot be excluded. The fact that these latent disturbances are not a rarity can be judged especially from results of a study conducted using the diagnostic model in a group of virtually healthy autotransport workers with considerable driving experience [150]. Let us present yet another example to illustrate the prospects for using the model in deciphering the mechanisms of reactions to angular acceleration. A study of nystagmic reaction to a series of sinusoidal rotation tests differentiated by amplitude established that in several cases, reaction asymmetry in patients (i.e. the magnitude and the sign of relative asymmetry) may vary depending on stimulus intensity [126]. /187
Results of the sinusoidal test demonstrating that K_{DP} is a characteristic whose sign and magnitude may be a function of stimulus intensity can be satisfactorily explained by comparing them with the results of a BT evaluated using the model. In practical terms, the approach worked as follows. The same subject was exposed to two tests -- bithermal and sinusoidal. BT results were used to find the model parameters and plot an NC EL graph. Then a low-amplitude sinusoidal test was "applied" simultaneously to each of the graphs. The difference in right and left EL's was found for the first sinusoidal stimulus half-period (i.e. the equivalent of the intensity of nystagmus in one direction) and then for the second sinusoidal half-

period (i.e. for a nystagmus in the opposite direction). "Reaction intensities" obtained in this way were compared with K_{DP} calculated as the normalized difference between intensities. Then stimulus amplitude was increased and the calculating procedure repeated. The result was a graph of K_{DP} as a function of sinusoidal stimulus intensity (cf. figure 55). With this approach, results obtained on paper qualitatively matched results from actual sinusoidal test. In other words, the model produced with a BT may be used to predict or analyze the results of a sinusoidal test.

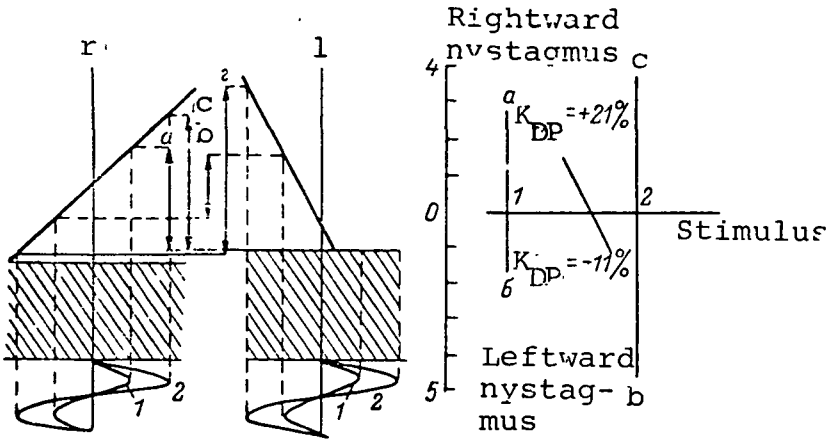


Figure 55. The phenomenon of asymmetry sign change in nystagmic reactions to sign-variable stimulation in a sinusoidal rotation test (graph on the right) and the possibility of using the diagnostic model (left) to study the mechanisms of this phenomenon (from [126]).

X-axis -- a series of sinusoidal tests differentiated by stand rotation amplitude: 1 -- the test with smallest amplitude; 2 -- with greatest (period in all tests in the series was identical, amplitude within each test was constant); Y-axis -- average intensity of right (a and c) and left (b and d) nystagmi. The asymmetry of these reactions within the framework of each test for mechanisms is viewed in comparison to directional preponderance during caloric tests. The model presents the pathology as a shift of the left AF characteristic and a background difference in EL. Sinusoidal stimuli act simultaneously on both labyrinths, creating a corresponding difference in the EL's of the two vestibular nuclear complexes -- right (r) and left (l). The difference in EL's in each case is defined first by model parameters and, second, by stand rotation amplitude. Obviously, responses to the first stimulus (a and b) differ significantly from responses to the second (c and d). Scales throughout are conventional.

The model also shows definite promise for research on a pathology associated with a change in physical properties of the cupula and intralabyrinthine fluid. These changes should undoubtedly show up in cupuloendolymphatic dynamics. For example, one might expect that a decrease in endolymph density, all other conditions being equal, would lead to an increase in cupuloendolymphatic shift, which in terms of the model would indicate an increase in characteristic slope. Finally, the model may turn out to be useful in studying vestibular recruitment, a phenomenon whose mechanism is still unclear -- even its very existence is questioned by some. /188

To summarize this chapter, the use of a diagnostic model substantially increases the information value of the bithermal test, making it possible to obtain answers to questions which traditional evaluation of the test does not provide:

	Evaluation of BT in Terms of:		
	Diagnostic Coefficients		Model
Diagnostic Task	K_{LA}	K_{DP}	Parameters
Observe pathology	+	+	+
Define location	+	-	+
Determine compensation	-	-	+
Eliminate pathology	-	-	+

Note several more regularities observed using the model and important for diagnostic nystagmographic research: 1) the presence of DP is not an unequivocal indication of the absence of compensation; 2) the equality of cool and warm nystagmus intensities on the healthy side is a nystagmometric indication of compensation; 3) if compensation exists, regardless of sign, DP originates peripherally.

Refining vestibulometric testing and finding ways to obtain information about the state of the vestibular function are among the most vital tasks of experimental-theoretical nystagmometry.

Since the bithermal test is now the only suitable test for diagnostic work to determine on what side and on what level the dysfunction exists, using the model to obtain additional information on the condition of receptors and nerve and vestibular nuclei is valuable. It seems relevant to recall in conclusion the words of V. I. Voyachek: "The problem of adding a quantitative aspect to caloric research is extremely acute. If this could be accomplished to the fullest, we would have an ideal way to measure vestibular function -- quantitative, and isolated for each ear and subject"([35], p. 153, paraphrased). One might hope that this study will contribute to solving the problem posed by a famous scientist more than 50 years ago.

Conclusion

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Quantitative research on nystagmus, begun at the time of visual observations and verbal description of reactions, already has its own history, which can be divided into several stages.

An important phase began with the development of nystagmography, since it was possible to analyze in detail nystagmometric characteristics and to study physiological mechanisms of nystagmus. At this stage, electronystagmography played an especially vital role and, because of its simplicity, accessibility and reliability, became popular and facilitated rapid accumulation of experimental data and clinical observations. The abundance of material required analysis and generalization, but this was hindered for a long time by the labor-intensity of manually processing nystagmograms. For this reason evaluation of nystagmus in everyday practice remains primitive to this very day.

The number of problems to be solved expanded considerably at the next stage, in which computers were used to analyze nystagmometric material. Now there exist several publications devoted to using computers in nystagmometric research (cf. e.g.: [60, 61, 86, 224, 266, 324, 355, 363, 364, 537, 564, 584]). However machine processing is primarily used in experimental nystagmometry; it is still not being used in standard applied (diagnostic) nystagmometry.

Widespread use of computer analysis of nystagmographic material in diagnosis requires automated systems which provide not only recording and quantitative processing of nystagmus, but also a final result in the form of a formal diagnosis. Of course, simplicity of operation and reliable performance of specialized devices must be ensured. How realistic is this prospect? From the standpoint of modern technical capabilities, these tasks are entirely realizable. For example, development of a device intended to solve type 1 diagnostic problems [130] described in chapter 3 is practicable. Success in developments of this sort and, especially, their benefits depend greatly on the extent to which medical men and biologists are prepared to turn the task over to engineers. In other words, identifying several problems including the mechanisms by which particular parameters form and the diagnostic value of /190
these parameters, comprehensive description of the norm and its variations, optimizing diagnostic algorithms, et al. take on special urgency with this approach.

Studies on existing automated systems which are intended for quantitative analysis of the nystagmic reaction have already been published (cf. e.g. [92, 105, 474, 518, 554, 573]). This can be viewed as a sign conclusively pointing to the beginning of a new stage in the history of the development of

nystagmometric research.

This stage presents certain difficulties. Automated analysis of nystagmograms (to obtain, for example, the functional of the nystagmus' dynamic characteristics) can still be done satisfactorily only when a rather long and regular nystagmus with clear boundaries between the slow and fast components of each impulse is evaluated. Only a few insignificant artifacts are permitted. In particular, optokinetic nystagmus in a healthy subject is one such reaction. In other words, not every nystagmus is even close to being suitable for completely automated analysis. Most nystagmograms recorded during pathological conditions are reactions which are difficult to analyze for several reasons -- pauses, reverse segments, tremors, pendular movements, and various artifacts. Under these conditions, automated analysis should be preceded by review of material with an experienced specialist who is to provide the required corrections before input into the computer, i.e. analysis essentially ceases to be automatic.

The near-term prospects for the development of nystagmometry are entirely worthy of optimistic assessment, because comprehensive study of vestibulo-oculomotor reactions (paths and centers, organization and control mechanisms, etc.) is being undertaken, not just by otoneurologists and physiologists, but by scientists in different disciplines -- space physiology and medicine, bionics, biophysics, cybernetics, and mathematics.

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